JEJUNOILEOSTOMY IN THE COMMUNITY HOSPITAL: 93 CASES FROM MONTANA

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I. INTRODUCTION

OBESITY AND MORBID OBESITY

A. DEFINITION AND COMPLICATIONS

For a condition that is of concern to so many people, from weight-conscious teenagers and their parents losing the battle of the bulge, to nutritionists and physicians analyzing trends and risks, obesity has proved to be remarkably difficult to define. Most of us use a loose inspection test, somewhat akin to the classic definition of an alcoholic as someone who drinks more than his physician does. Mayer states that

> "...the only possible logical definition of obestity rests on defining at what point the proportion of body weight represented by fat becomes abnormally high. Exact definition of this limiting value is arbitrary." (118)

He suggests that when fat makes up 30% of body weight, a person is obese. Others have accepted this figure for women, but would allow a man's body weight to be only 25% fat.[19]

The difficulty that arises is how to measure body fat. Direct measures of body fat in cadavers are accurate but have limited applications to clinical research for obvious reasons. Indirect measures break down into three general categories. First, isotopes can be used to estimate body water or lean body mass, from which figure an approximation of body fat can be derived. Second, body density studies, involving weights both in and out of water, give fairly accurate estimates of body fat because of the different densities of fat and lean body mass. Finally, various anthropometric means are used: namely skinfold thickness, height, and weight. Because of inherent difficulties in technique, isotope studies and densitometry are not feasible for routine use. For practical purposes, antropometric means are almost universally employed. Triceps skinfold thickness is held to be a more direct measure of body fat than the ratio

of body weight to a somewhat arbitrary "ideal" weight. However, reproducibility is a problem: there may be large variations in measurement depending upon the calipers used and pressure applied. Many investigators have fallen back on tables of "ideal body weight" prepared by insurance companies. The "ideal weight" is an arithmetic mean of weights of insured persons of a given height and sex. One can easily fault these tables: the insured population is skewed toward the wealthier members of society and occupational differences are ignored. Weights are taken with the individual "ordinarily dressed," and heights are often recorded with the shoes on. Since all these tables originate in the United States, applicability in other countries is questionable.[97,118] With all their weaknesses, however, the insurance company tables are convenient to work with and are used widely. Accepting the limitations of the "ideal weight," obesity has been defined as a weight greater than 20% over ideal body weight for height.[16] The term morbid obesity has been used for those obese subjects whose weight is twice ideal or greater than 100 pounds over ideal.[146,172]

The incidence of the somewhat arbitrarily defined condition of obesity is quite surprising. The U.S. Public Health Service estimates that anywhere from 25 to 45% of Americans over age 30 are more than 20% overweight. Similarly 2 to 15% of children are obese, as defined by a weight 40% over the median for height.[205,208] In both children and adults, obesity is more common in the lower socioeconomic classes: for women, "extreme overweight" is seven times as frequent in the lower socioeconomic classes as in the upper classes.[90] Age is also an important factor. In all studied species of mammals, as the mature animal ages proportionately more of the body weight goes to fat, even without an increase in body

weight.[118] Forbes and Reina have shown that lean body mass, as measured by ^{40}K, declines with age in adults, and the rate of this decline increases with advancing years.[55] Not only does the proportion of fat increase with age, but in the U.S. and many other developed countries body weight also increases after age 25. This has important implications in evaluating the risks associated with obesity -- obese people will tend to be older and thus at increased risk, for example, for cardiovascular disease.[98]

What exactly are the risks associated with obesity? Insurance companies have long been charging an extra premium for obesity because of excess mortality. According to insurance statistics, overweight men have a mortality rate 1.5 times that of standard insured risks. Those who are moderately overweight (30-35% over ideal weight) have a mortality rate 1.4 times normal; men who are 40-55% over ideal weight have a mortality rate 1.8 times normal.[111] Mortality rates for obese women are similar but less dramatically increased. When the diseases contributing to this excess mortality are examined specifically, the main offenders are found to be cardiovascular disease, diabetes, and gallstones.[12] Obese men with a moderate elevation in blood pressure demonstrate a 60% increase in mortality rate when compared to their normal counterparts. Men with severe hypertension who are markedly obese have a mortality rate 3-4 times standard.[143] Mortality from cardiovascular disease is 1.5 times normal in obese men and 1.75 times normal in obese women. Death rate from diabetes is almost 4 times standard in both obese men and women. Mortality rate from cirrhosis, gallstones, and appendicitis is approximately twice normal prevalence rates.[111] With weight reduction, insurance statistics indicate that mortality rates decrease. In moderately obese men and women who were re-rated for insurance after weight loss,

mortality rate fell from 1.4 times standard to 1.1 and 0.9 respectively.[111]

Some caution must be used in interpreting insurance statistics. The 1959 Build and Blood Pressure Study concluded that any degree of excess weight was a risk to health, but re-evaluation in 1966 demonstrated that the increased mortality was seen mainly at levels of extreme obesity.[90] It is of interest, then, to review current medical thinking regarding the complications of obesity.

Hypertension. A number of studies have found hypertension to be more common among the obese, particularly the morbidly obese.[20,67,98,109,141,217] The Framingham Study revealed that both blood pressure and weight increase with advancing age in women. Using age-adjusted groups, it was found that average BP increased with relative weight (patient's weight/standard weight) in both men and women, but the correlation of systolic BP and relative weight was only a modest one ($r = 0.3$, $p < 0.05$). However, the relative weight correlated more closely with systolic BP than did either the triceps skinfold measurement or the upper arm girth. Another important observation was an increased prevalence of obesity (relative weight > 120) among those subjects who were hypertensive (systolic blood pressure > 160 and/or diastolic blood pressure > 95).

TABLE 1
(modified from Kannel et al.[91])

PER CENT OBESE

ENTRY BLOOD PRESSURE	AGE (Years) 30-39	40-49	50-59
Normal	2.1	4.1	2.9
Borderline	12.9	7.5	6.5
Hypertensive	18.8	16.0	13.1

Trends for each age group significant ($p < 0.05$)

Initially normotensive obese subjects were more prone to develop hypertension than their counterparts with normal weight. Eight years after entry into the study the incidence of hypertension in originally normotensive obese subjects was 3.2 times expected ($p < 0.05$). In fact, "subsequent development of 'hypertension' was shown to be related not only to gross 'obesity' but to relative weight, per se, as determined on the initial examination."[91]

Weight loss in both the obese and nonobese over the 12 year follow-up period was associated with a fall in blood pressure in both men and women, and weight gain with a rise in blood pressure.[91] Fletcher studied a group of obese hypertensive women (systolic BP >150 or diastolic > 90) who lost weight. Those with systolic hypertension who lost more than 14 pounds (average 33 pounds) had a mean fall in systolic BP of 33 mm Hg.; those with diastolic hypertension had a mean decrease in diastolic BP of 16 mm. These changes were statistically significant when compared to the hypertensive women who lost less than 14 pounds.[53]

There is evidence, then, that the obese are prone to hypertension (essential hypertension, not renovascular or secondary hypertension[67]). With weight loss blood pressure tends to fall. Kannel also reports that lean hypertensive subjects are more likely to become obese than lean normotensives, leading him to conclude that the relationship between adipose tissue and hypertension is "neither simple nor direct."[91]

One specter that has been raised with regard to all studies of obesity and hypertension is the possibility of an artifactual elevation in blood pressure due to cuffs too small for obese arms. That such cuff artifact is possible even in nonobese patients is clear from a report by Orma et al., in which all patients had elevated blood pressures the

first day that a new cuff was in use. The difficulty was related to a short bladder size in the new cuffs.[142] Numerous studies have examined the relationship between direct and indirect measurement of blood pressure. Alexander compared cuff pressure and intra-arterial pressure in a group of obese patients and found identical values 50% of the time; the other 50% split equally between cuff pressures higher and those lower than direct.[1] Berliner also recorded simultaneous direct and indirect blood pressures. He found minor discrepancies in both directions in the lean and moderately obese, and a considerable error of the indirect measurement in the extremely obese, in whom both systolic and diastolic pressures tended to be overestimated.[10] However it should be noted that his cuff length was 20 cm. -- 3 cm. shorter than the cuffs which created the artifact in normals noted by Orma.

The Framingham Study addresses this issue by utilizing forearm blood pressure and by reanalyzing the data with obesity defined in terms of arm girth. Blood pressure readings of hypertensive patients (standard cuff) were repeated using the cuff around the forearm and auscultating at the radial artery. The loss of hypertensive readings using this technique was minimal: basically the equivalent of a repeat blood pressure reading on the upper arm. Kannel points out that normotensive obese subjects, who presumably had fat arms, had a definite tendency to develop hypertension on follow-up. When patients were reclassified by arm girth, the frequency of hypertension in obese patients was similar with or without large arm girth; conversely, the groups with big arm girths had a variable frequency of hypertension depending upon relative weight. Kannel concludes that "arm girth produces no independent effect on blood pressure."[91] Thus while a cuff artifact may exist (particularly in the morbidly obese),

the evidence is equivocal as to its significance. The use of a thigh cuff in the obese does not seem to be necessary when forearm blood pressures are so much more convenient.

Cholesterol and triglycerides. The correlation between obesity and elevated cholesterol tends to be weak.[139] Montoye et al were able to demonstrate a small correlation between serum cholesterol and skinfold thickness in men under 50 years of age.[125] Mann's data reveals a slight correlation of obesity with cholesterolemia.[109] Despite the poor correlation, induction of obesity by overeating results in elevated lipid levels.[109] Twenty-five to forty percent of morbidly obese patients have elevated cholesterol levels.[9,20] Cholesterol levels decline with weight loss, sometimes drastically.[2,109,139]

Plasma triglyceride levels in man are intimately related to carbohydrate intake. High carbohydrate diets increase and carbohydrate restriction decreases circulating triglycerides.[130,56] This effect of carbohydrate intake on triglycerides may be mediated by changes in plasma insulin.[48] There is a significant correlation between fasting insulin and fasting triglyceride ($r = 0.43$, $p < 0.01$).[139] Olefsky postulates that elevated insulin levels in obesity augment hepatic triglyceride synthesis, thereby leading to hypertriglyceridemia. After weight loss averaging 10.9 kg. in moderately obese subjects (mean relative weight 121), plasma triglyceride decreased markedly (319 → 180 mg/100 ml, $p < 0.0001$) in conjunction with a similar decline in plasma insulin.[139] It has not been established whether alterations in triglyceride homeostasis in obesity are related directly to carbohydrate intake or to hyperinsulinemia.

Coronary heart disease. Insurance statistics show that a large proportion of the increased mortality in obese subjects is due to

cardiovascular disease.[12,111] Master et al demonstrated that almost twice as many men with angina, acute coronary insufficiency, and acute coronary occlusion were overweight or obese.[116] The Framingham Study shows an increased incidence of angina and sudden death in obese men but not obese women. Excluding men with systolic hypertension or hypercholesterolemia, the risk of developing angina or sudden death was twice normal in those who were obese (relative weight > 120). The risk of myocardial infarction, on the other hand, was found to be related primarily to hypertension and hypercholesterolemia, and not to excessive weight.[92]

The relationship between obesity and coronary heart disease has come under close scrutiny in recent years. Keys criticized the Framingham report for lumping all ages together. Applying multivariate analysis to the original data, he come to the conclusion that relative weight is a risk factor for coronary heart disease in men of 40-49 years, but not for ages 30-39 or 50-59. He also pointed out that the increased risk is for heart disease diagnosed by soft criteria (i.e., angina).[98] The implication is that clinicians are overdiagnosing nonspecific symptoms in the obese patient as coronary heart disease. A longitudinal study in Evans County, Georgia was unable to demonstrate a relationship between overweight and sudden death.[77] Chapman et al could not find a consistent association between angina and myocardial infarction and the weight index (height in inches/cube root of weight in pounds).[33] Mann concludes that coronary heart disease is related to hypertension, not obesity per se.[109]

Cerebrovascular accidents. Both obesity and weight gain after age 20 are associated with an increased incidence of cerebrovascular disease. According to the Evans County, Georgia Study the lowest incidence of

strokes occurred in subjects who weighed under 150 pounds at age 20 and gained less than 30 pounds thereafter. Similarly the highest incidence was seen in the group weighing over 150 pounds at age 20 who gained more than 30 pounds since. Weight at age 20 and weight gain after 20 exerted independent effects on cerebrovascular disease. Heyden postulates that the effect of weight gain on subsequent stroke is mediated through the accompanying elevation of blood pressure. Weight in young adulthood acts through another, as yet unidentified mechanism.[77]

Glucose intolerance. The association between obesity and glucose intolerance has been recognized for many years. Fifty to sixty percent of obese subjects have an abnormal glucose tolerance test.[93] More importantly, 75-85% of adult-onset diabetics are obese. The likelihood of developing diabetes is 3 times normal in anyone 15% or more over ideal weight, and 8 times normal in those who are 25% or more over ideal.[140]

In 1963 Karam et al observed that obese subjects with normal glucose tolerance tests had elevated basal serum insulin levels compared with nondiabetic normals. Nine of the 10 obese subjects had prolonged elevated insulin levels in response to a glucose load.[93] Bagdade et al demonstrated a correlation between the fasting level of insulin and per cent ideal body weight, but not between fasting insulin and glucose intolerance. The insulin response to a glucose load was proportional to fasting insulin levels. Both obese and nonobese diabetics had a lesser increment in insulin after glucose than did obese and nonobese nondiabetics.[4] Perley and Kipnis showed that serum insulin at comparable glucose levels was lower in obese diabetics than in obese nondiabetics.[150] Genuth measured insulin production and estimated a normal value at 31 units/24 hrs. Obese diabetics produced about 46 units/24 hrs. and

obese nondiabetics 114 units/24 hrs.[61]

Most obese patients are resistant to insulin, as a consequence of tissue insensitivity rather than faulty synthesis of a circulating antagonist. The response of obese subjects to exogenous insulin is invariably reduced. Recent studies suggest that this effect may be mediated by changes in insulin receptors. Studies in obese animals have shown a decreased number of insulin receptors per adipocyte, and evidence is mounting that obese humans have fewer insulin receptors both in circulating monocytes and adipose tissue.[5,135] Whether such important insulin target tissues as the liver and muscle are similarly affected has yet to be determined.[138] Although a decreased number of receptors might be expected to produce the hyperinsulinemia observed in obesity, some observers have suggested that insulin may control the number of its own membrane receptors.[135,43] According to this theory, increased carbohydrate intake is followed by increased insulin output, which decreases the number of receptors on target cells. Thus hyperinsulinemia may actually be the primary event inducing insulin resistance.

A decrease in the number of insulin receptors on a cell does not necessarily produce a decreased response to insulin. Maximal stimulation of glucose uptake occurs when only a small proportion (about 10%) of insulin receptor sites are occupied.[137] A defect distal to the membrane binding of insulin has been postulated to explain insulin resistance in some cells. Olefsky has found an abnormally low rate of glucose oxidation in adipocytes from obese rats.[137] The defect has been localized to the hexose monophosphate shunt.[138]

Thus obesity seems to lead in some way to insulin resistance, either via decreased number of insulin receptors or through a more distal mechanism.

Some obese patients with hyperinsulinemia have normal glucose tolerance. The obese diabetic, although hyperinsulinemic compared to normals, produces less insulin than the obese nondiabetic. With weight loss insulin resistance improves[48], and the available insulin of the obese diabetic may be adequate for his needs. With continued obesity and diabetes, one can anticipate all the cardiovascular, renal, and ocular complications seen in nonobese diabetics. Certainly diabetes is a significant, life-shortening complication of obesity.

Pickwickian Syndrome. Burwell originally labeled the syndrome of extreme obesity, hypoventilation, somnolence, polycythemia, and right ventricular failure a "Pickwickian Syndrome", after the fat boy in Dickens' Pickwick Papers.[30] Hypercapnia is responsible for the somnolence and occasional twitching; hypoxia leads to secondary polycythemia, pulmonary hypertension, right ventricular hypertrophy, and eventually right heart failure. There is controversy over the underlying cause of the hypercapnia and hypoxia. An increased work of breathing has been postulated to lead to hypoventilation. Pickwickian patients tend to have a low expiratory residual volume, vital capacity, and total lung capacity.[30,70] (These abnormal lung volumes may be related to increased intraabdominal pressure.) Compliance is reduced as the lung approaches expiratory volume[30], and the work of breathing is greater. It has been suggested that altered mechanics of breathing alone should not lead to hypoventilation. Of interest in this regard is that the ventilatory response to both hypoxia and hypercapnia has been shown to be markedly reduced in obese hypoventilators.[229] With weight loss the sensitivity of the respiratory center to CO_2 returns to normal. Weight loss does not, however, correct the depressed ventilatory response to hypoxia.[30,229] Fried et al

have suggested that ketosis, rather than weight loss per se is responsible for the improvement in CO_2 sensitivity, but their patients were not overly Pickwickian, nor did patients serve as their own controls.[58]

It is likely that both extreme obesity and an abnormal ventilatory drive are necessary to produce hypoventilation.[229] Weight loss has a dramatic effect. When a certain weight is reached symptoms disappear, only to return when weight creeps above this threshold level. If weight loss can be maintained patients are apparently cured.

Fatty liver. Abnormal LFT's are common in the obese, particularly sensitive, nonspecific indices. BSP retention is abnormal in 76-100% of cases, according to reported series; thymol turbidity and cephalin flocculation are also frequently abnormal.[9,218,228] Some degree of fatty infiltration can be demonstrated on liver biopsy in 60-100% of obese subjects.[9,102] Zelman described moderate to marked fatty changes in 10 of 19 obese noncirrhotic subjects. Those with longstanding obesity were more likely to have degenerative parenchymal changes as well.[228] Kern examined 151 liver biopsies of morbidly obese patients undergoing intestinal bypass surgery and found fatty metamorphosis in 94%. Changes of periportal fibrosis were present in 42 of the 151 cases, with moderate or marked fibrosis in an additional 8. Three cases were suggestive of early portal cirrhosis, and 3 showed changes characteristic of Laennec's cirrhosis. Kern suggested that this spectrum of fibrotic changes might represent progression from the original "benign" lesion of fatty infiltration.[96]

Although insurance statistics show that more obese individuals die of cirrhosis[111], there is no proof of a causal relationship. Fatty infiltration secondary to obesity can be mobilized over 4 to 6 weeks with

weight loss.[102] Westwater and Fainer have noted improvement in abnormal liver function tests in several obese patients after weight loss to within 15% of ideal weight.[218] Thus both the pathological changes of fatty liver and the mild abnormalities of liver function appear to be reversible. It is possible that obese nonalcoholics develop cirrhosis after long-standing fatty infiltration of the liver, but it is doubtful that this occurs with any great frequency.

Other medical complications. Obesity is a major risk factor in pregnancy for both mother and child.[109,111] In one series, 12% of maternal deaths occurred in women who weighed over 200 pounds.[107] The incidence of gallbladder disease is 2 to 3 times normal in the obese.[20] Obesity is associated with carcinoma of the endometrium.[176] The risks of anesthesia and surgery are greater for those who are overweight. Osteoarthritis, affecting mainly the back, hips, knees, and ankles, causes a great deal of morbidity, and the extremely obese are more likely to develop these degenerative changes.[95] Lymphedema, venous stasis, and intertriginous dermatitis are frequent problems.[28,217] Finally obese individuals are involved in more accidents.[220]

Psychosocial complications. Psychiatrists have had much to say about the obese personality, concentrating on neurotic characteristics. Rubin's obesity profile includes an obsessive preoccupation with food; an excess of all oral activities (not only eating and smoking, but talking, smiling, and laughing); eating binges followed by rationalization and then guilt; and finally a distorted body image.[24] Others have found that the obese are more prone to depression, which they tend to accept in a passive way rather than struggling against it.[36] Stunkard's careful studies have demonstrated only two behavioral disturbances clearly related

to weight: overeating and a body image distortion. He found that many of his patients were preoccupied with weight. They felt that their bodies were grotesque and disgusting, and were convinced that others felt the same contempt. Emotionally healthy adults did not have a body image disturbance, but emotionally unstable adults whose obesity had begun in childhood or adolescence commonly did. Weight loss did not have any effect on the distorted body image, but psychotherapy was thought to be helpful.[199,201]

It is not surprising to find that many obese people believe that their bodies are disgusting to others. Certainly in our society there is a stigma attached to being obese. Women in particular are supposed to be thin to conform to our cultural values of youth and sexuality. In cultures which define femininity in terms of mothering and childbearing, what we call obesity is considered perfectly normal. Obesity carries less of a social disadvantage for men in Western society. As Kalisch states,

> "The appearance of men is important, but financial status, educational achievement, and occupation affect his value more." (90)

It is important not to discount the significant emotional complications of obesity. Call this what you will -- a body image distortion or a neurotic personality -- it simply reflects societal discrimination against those who are overweight. Even the most stable individual cannot help but be affected in both work and social situations. The "happy-go-lucky" outlook worn by many overweight people covers the scars from years of emotional trauma. Weight loss means more than a number of pounds or fewer medical risks: it means normality, acceptance, a chance to start all over. At the same time it represents an unknown to be feared. To successfully serve the patient, the physician must deal with all aspects of the problem of obesity.

B. ETIOLOGY

Despite the common lay belief that most fat people have an endocrine problem, very few of them actually do. In a small proportion of cases, obesity may be attributed to genetic, central nervous system, or endocrine disease. Clearly genetic types of obesity exist: the Laurence-Moon-Biedl syndrome, hyperostosis frontalis interna, the Prader-Willi syndrome, are all typified by marked overweight. CNS pathology (hypothalamic tumors, Fröhlich's syndrome, and trauma) can lead to obesity. The endocrinopathies that are blamed so frequently include islet cell dysfunction (varying from hyperplasia to insulinoma), chromophobe adenomas of the pituitary, Cushing's syndrome (primary and iatrogenic), hypothyroidism, and pseudohypoparathyroidism.[19,119] (It is interesting to note that in hypothyroidism and pituitary disorders, weight loss from dieting has at times been found to improve and even reverse the signs of glandular insufficiency, suggesting that low levels of hormone were present but inadequate for large body size.)[227]

Genetic abnormalities, aside from those syndromes mentioned, seem to have a more general role to play. In rats there is clear mendelian transmission of obesity, and the obesity of yellow-coated mice can be assigned to a dominant gene. The obese hyperglycemic syndrome in mice is attributable to a single recessive gene.[118] In humans obesity in childhood has been found to be associated with an increased incidence of adult obesity.[34] Identical twins have closely correlated body weights.[109] Sixty-nine to eighty-two per cent of obese subjects have an obese parent.[72,118] However environmental factors have not been controlled in any of these studies and the role of genetics is still not clear.

At the most basic level, obesity is always the result of a positive energy balance.[23] Either decreased energy expenditure or increased caloric intake can lead to such a positive energy balance. Several groups have concentrated on decreased physical activity in the obese, suggesting that the body's regulation of input to output does not function normally at very low levels of activity. Mayer et al demonstrated that, in general, food intake decreases with decreasing activity; however, at low levels of activity, diet may not be curtailed proportionately.[120] There are a number of difficulties with this ambitious study, including the fact that diet was determined by history only. Although studies have shown that the obese are less active than normals (particularly obese women), it is impossible to conclude that the decreased activity is primary, and not a secondary effect of obesity.[36,89]

An increased efficiency of metabolism has been postulated as a mechanism for decreased energy expenditure. It has been assumed that basal caloric expenditure is constant over the entire range of caloric intake. However, when Bray measured resting energy expenditure after a semi-starvation diet in 6 obese women, he found a decrease of 15% from baseline. He postulated a shift in intracellular glucose metabolism away from the energy-wasting glycerophosphate cycle (in which reducing equivalents are shunted into mitochondrial oxidative phosphorylation at the flavoprotein level, yielding only 2 ATP instead of a potential 3 ATP). He was able to demonstrate a decreased amount of both soluble and mitochondrial glycerophosphate dehydrogenase (the key enzyme) in subcutaneous fat biopsies from patients under caloric restriction.[17] Assays of the enzyme in a second study showed reduced levels in obese patients compared to normal controls, with a further drop on dieting.[59] Animal studies suggested

that the enzymes of the glycerophosphate cycle were partly controlled by thyroid hormone, which led Bray to treat his obese patients with tri-iodothyronine.[18] Large doses were required, however, and it is difficult to attribute the entire weight loss to an increased activity of glycerophosphate dehydrogenase. The finding of a decreased basal caloric expenditure when intake is reduced certainly has implications for dieters -- namely, weight loss will not necessarily occur as quickly as predicted.

The thermal dissipation, or "Luxuskonsumption," theory has also been resurrected to explain a decreased energy output. Several amazing studies of obesity induced in normals by massive overeating have revealed an increased heat production that dissipates much of the excess caloric intake and results in a weight gain remarkably less than predicted.[109,123,124] Basal metabolic rate remains unchanged, and 24 hour oxygen consumption must be measured to appreciate the increased heat production, which occurs primarily after meals. The thermic response is shown to be proportional in both size and duration to the caloric content of the meal and is more marked if the subject exercises after eating (even excluding the heat loss from exercise).[124] Proponents of this theory hypothesize that the obese have a less than normal thermal dissipation in response to increased caloric intake, leaving them with a positive energy balance.

Caloric intake is controlled by a number of factors: the hypothalamus, behavioral patterns, psychological conflicts, and social customs. The ventromedial nucleus of the hypothalamus has been found to be the satiety center in humans, with a hunger or food-seeking area located laterally. There are a number of theories as to how the "appestat" works, including (1) the detection of small increments in heat produced by metabolism of

food; (2) sensitivity to changes in glucose concentration (glucostatic theory); or (3) nervous stimuli.[15,109,118] Although gross lesions in the ventromedial hypothalamus in animals, produced by gold thioglucose or a stereotaxic lesion, have induced massive obesity with a complete absence of satiety[109], it is difficult to apply these studies to humans. One study that relates adult obesity and lean-ness to periods of plenty or famine in early life postulates that the hypothalamus is "set" early in life depending on the available food supply.[158] Such subtle defects in the "appestat" are beyond our present capabilities of detection and remain theoretical.

There is evidence that eating patterns in the obese differ from the norm. Schachter found that the obese were less responsive to internal cues regarding satiety and tended to make decisions on food intake depending on external cues: i.e., how much food was available, how good it was, and how easy it was to obtain.[168] Stunkard suggests that these stimulus-bound people must make conscious choices about eating, rather than relying on an unconscious, internal regulation which for some reason does not function properly.[198] Clearly this is not incompatible with theories of an hypothalamic abnormality.

Psychiatrists have found it difficult to sort out the psychiatric problems created by obesity from those leading to obesity. Basically there is no direct evidence linking emotional factors to increased food consumption and obesity.[204] However, psychological theories of obesity abound. Freud saw it as a regression to the oral stage. Brosin expands on the symbolic value of obesity: a big body can be viewed as a fortress or may stand for a desired pregnancy.[22] Food may become a substitute for inadequate parental love and protection[227], or be used to resolve

tension. Some have described obesity as an addiction, but as Swanson and Dinello point out this results in a real therapeutic dilemma, since total abstinence is impractical![203,204]

Sociocultural factors contribute to increased caloric intake in a significant way, as has already been mentioned. Ethnic background has a major influence on the value attached to body weight, as does socio-economic status.[66] As Goldblatt et al state,

> "It is now apparent that obesity can no longer be viewed as simply an abnormal characteristic of the individual. It must be viewed as one of the possible, and not too infrequent, normal responses of persons in certain sub-groups of society to the perceived expectations of their social milieu." (66)

The relative importance of each of the above-mentioned factors in producing an intake inappropriate to energy utilization is impossible to determine, and probably varies from case to case. With the exception of behavior modification techniques, the therapeutic approach to obesity is to ignore the underlying factors and concentrate on correcting the positive energy balance.

C. MEDICAL MANAGEMENT

Dieting has been the mainstay of medical management of obesity for years. A reasonable goal is to reduce caloric intake sufficiently to lose 1-2 pounds per week. One pound of fat is equivalent to 3500 calories (fat = 9 cal/g = 4000 cal/lb; however body fat is 15% hydrated). Thus a deficit of 1000 calories daily should lead to a weight loss of 2 pounds weekly.[15] However the basal metabolic rate decreases as caloric intake is reduced [18,225], and thus a greater reduction in caloric intake may be required to sustain comparable rates of weight loss.

There are innumerable diets: water diets, grapefruit diets, low carbohydrate diets, high protein diets. Diet composition is important primarily in terms of fluid loss. Subjects on a low carbohydrate diet lose more weight in the early stages of dieting than those on a higher carbohydrate intake. Water loss accounts for this entire difference.[225] The rate of fat loss is comparable in isocaloric diets, irrespective of the proportion of carbohydrate, fat or protein in the diet. However a disconcerting weight gain due to fluid retention may be seen on changing to a diet with a greater amount of carbohydrate.[78,225,227]

In the most important aspect, all diets are alike: they are generally unsuccessful. Review of studies of successful weight loss reveals that perhaps 25-30% of subjects were able to lose over 20 pounds, and only 5-8% lost over 40 pounds.[18,51,200] The single exception was Feinstein's series. He treated 106 patients of varying degrees of obesity with a 900 calorie formula diet. The regimen included weekly or biweekly follow-up and an initial lecture to explain the diet. Thirty-five per cent quit within 4 weeks, but were included in analysis of the data. Weight

loss of over 20 pounds was achieved in 59% of patients, and 31% lost over 40 pounds.[51] Feinstein attributed the success to the simplicity and inflexibility of the diet; however he also believed that psychological factors were very important.

Weight loss can be achieved, albeit in a small proportion of those dieting. More important is whether weight loss is maintained. In a long-term follow-up of 27 obese patients 14 years after successful weight loss, 22 had regained all the lost weight (and 3 of them had put on an additional 10% of body weight) while 5 had maintained a weight loss of approximately 15% of body weight, although they were still overweight.[185] Of 12 patients in Stunkard's series who lost over 20 pounds, only 6 were "successful" one year later (they weighed at least 19 pounds less than when they started to diet). Two years after the diet, only 2 continued to be "successful."[200] Weight maintenance in Feinstein's formula diet was typically unsuccessful: of 12 who reached their standard weight, 6 had regained $\geq$ 30% of the lost weight in one year. From another 36 who were able to lose over 30 pounds, follow-up was available on 26. Fourteen had regained $\geq$ 30% of the lost weight. This left a total of 18 from the group of 106 who were able to maintain a reasonable weight loss for one year.[51]

As Bray states, "if there was an effective diet, there would be no need for the continuous introduction of new diets," nor for what Mayer refers to as the "rhythm method of girth control", i.e., weight loss on a diet followed by relapse and another attempt at weight control when a new diet is advertised.[18] After concluding that no diet works consistently for outpatients, Feinstein analyzed factors leading to successful dieting. Differing results for similar diets are largely related to patient

motivation and the strength of the doctor-patient relationship.[50]

A number of adjuvants to diet therapy are available. Exercise proponents have calculated that one hour of brisk walking uses 350 calories, and a one hour "work-out" uses 800 calories; thus a daily walk, or a work-out four times a week, should result in weight loss of about a pound a week.[110] Some worry that exercise increases appetite, but this generally is not enough to interfere with weight loss. Exercise is useful in improving muscle tone and contributing to a general sense of well-being.[176] It is an important part of the dietary regimen, but is seldom used alone for weight regulation.[50]

A variety of anorexiant agents have been introduced to assist the dieter. A double blind study using a mixture of dextroamphetamine and prochlorperazine in obese women concluded that those receiving the drug combination experienced a greater weight loss over 6 weeks than those receiving placebo and those who did not get any medicine. It is interesting that 69% of those receiving placebo described a decrease in appetite, compared to 86% on the active drug, a difference that was not statistically significant.[159] Because tolerance to anorexiant drugs develops, Silverstone and Solomon designed a double blind trial of diethylpropion, a long-acting agent, given daily in alternate months. Controls received placebo in alternate months and all were placed on a low carbohydrate diet. Only 11 of the original 32 completed a full 12 months trial, and there was no significant difference in weight loss between the 2 groups.[182] Many people feel that these drugs are of questionable value.[50,109] Although they may be useful short-term adjuvants to diet, none of the anorexiant agents is helpful in the maintenance of weight loss. All these drugs must be used with caution, not only because of their abuse potential,

but also because deaths have been reported.[86]

Hormone therapy, particularly with thyroid, has been suggested to help the dieter lose weight. (It should be noted that thyroid function is normal in most of the obese.[9]) Thyroid hormone (either T_3 or T_4) in pharmacologic doses does lead to a temporary weight loss, but the subject tends to lose lean body mass rather than fat. Once the hormone is discontinued the weight is quickly regained. There are also significant risks to treating euthyroid subjects with thyroid, most notably cardiac arrhythmias.[160] HCG (human chorionic gonadotropin) as a daily injection has been said to have a significant effect on weight loss. Studies have been poorly controlled, however, with conflicting results.[78] Growth hormone has also been used, with equivocal success.[160] It appears that weight loss associated with hormone therapy is due to the accompanying caloric restriction.[50]

Group and individual therapies have been used as an adjunct to diet. "Weight Watchers" and "Overeaters Anonymous" are informal groups of people with weight problems. TOPS ("Take Off Pounds Sensibly") is a similar nonprofit organization that uses social pressure to encourage weight loss. Weekly meetings center around the weigh-in, in which weight loss or gain is announced to the audience, to be greeted by the appropriate applause or hisses. There is no controlled study of the TOPS program, but apparently if a new member stays (50% drop out within 6 months), he or she will lose some weight. Although the group views overweight as an emotional problem, most of the individual members avoid mental health resources.[211]

Group therapy led by trained psychiatrists has been no more successful than diet alone in producing weight loss. Buchanan's study, in fact,

demonstrated a weight gain over the first 6 to 9 months, attributed to resistance to the exploration of internal conflicts.[24] Most individual psychotherapy has concentrated on depressive symptoms that occur during dieting and following weight loss, relating this to oral deprivation, unresolved tension, or a failure of weight loss to solve all the individual's life problems.[65]

One promising contribution from the behavioralists is the application of behavior modification techniques to the problem of weight loss. Overeating is the only behavioral characteristic consistently associated with obesity.[224] If behavioral disorders are learned responses, then in theory these responses can be unlearned: the environment can be modified to strengthen "good" eating habits and weaken or extinguish "bad" habits. In general, food is removed from all rooms except the kitchen; all food, except salad, is kept in an unprepared state (to cut down on compulsive eating); eating is made a pure experience, apart from listening to the radio or watching TV. In Stuart's original group of 10, 8 lost over 20 pounds and 2 lost over 40 pounds.[194] Fifty-three per cent of Penick's 15 patients lost over 20 pounds, and 13% lost more than 40 pounds. At follow-up ranging from 3 to 6 months, 27% had lost more than 40 pounds.[149] These results compare favorably to the best series of dietary management alone. However numbers are small, and further study is required to fully evaluate the success of behavior modification.

In-hospital fasting and semistarvation diets (300-600 calories/day) have been quite successful in producing weight loss. The restricted environment generally assures caloric deprivation. On a total fast a weight loss of 3/4 to 1 pound per day can be expected.[15] This mainly represents metabolism of adipose tissue. The body's carbohydrate stores

are so small as to make a negligible contribution to weight loss. Protein is lost initially, but protein dissolution progressively declines and soon represents only a small portion of the total negative caloric balance.[214] Administration of small amounts (200-300 calories) of glucose, L-alanine (a major glucose precursor), or casein has been shown to minimize protein loss.[62]

Fluid and electrolyte depletion can be major in the first days of fasting or semistarvation, resulting in postural hypotension. Although aldosterone and acidosis may contribute to sodium wasting, it is likely that other factors are more important. Sigler postulates that sodium loss during fasting is obligatory as cation coverage for metabolically generated anions (primarily ketoacids). Refeeding with glucose leads to a parallel decrease in excretion of sodium and anions. When adaptive renal ammonium excretion increases, sodium loss is reduced.[181] Thus after the first week of fasting, sodium losses are small.[214] Hypoinsulinemia[42] and increases in glucagon[167,189] during fasting may also be important contributing factors. Potassium is lost in the urine at an initial rate of 40-45 mEq/day.[214] Renal adaptation is somewhat more gradual than with sodium, and is only partial. A loss of 15-20 mEq potassium per day can be expected, leading invariably to depletion of whole body K^+ and often to a fall in serum K^+. Losses of Ca^{++} and Mg^{++} are small and generally insignificant.[19]

Ketosis occurs in patients undergoing severe carbohydrate restriction or fasting, occasionally leading to mild nausea and an unpleasant taste in the mouth.[204,203] Hyperuricemia always develops as ketoacids compete with uric acid for transport by the proximal tubule. With refeeding the uric acid falls only gradually, even though ketosis disappears rapidly.[101]

Most patients tolerate a fast or semistarvation diet well. Supplementation with vitamins, folate, and potassium is routine. Intake of noncaloric fluids is encouraged. Patients with a history of gout are placed on allopurinol.[18] Symptoms are usually confined to the first few days of fasting (mild headache, nausea, dizziness) and resolve spontaneously, although postural hypotension may persist. Complications do occur, including electrolyte imbalance, leukopenia, anemia, renal stones, hair loss, and muscle wasting, as well as death on rare occasions (secondary to lactic acidosis, muscle depletion, and arrhythmias).[101,190]

Success has been equivocal: weight loss occurs consistently, but maintenance at the new level rarely lasts long. Swanson and Dinello found only 16% "partial success" in a follow-up of 1-50 months in a group of fasted patients (56% had regained all the lost weight; 28% were lost to follow-up).[203] Follow-up by questionnaire in another series of fasted patients revealed weight gain in 33% of respondents; 46% continued to lose weight, and 21% remained the same. However only half the initial subjects returned their questionnaires, and they tended to be ones who had been most recently discharged from the hospital.[84] MacCuish and Munro's intial experience with fasting was discouraging: mean weight loss during the fast was 26.7 pounds, and mean weight gain on follow-up (averaging 14 months later) was 28.5 pounds. However, 4 of their 23 patients did manage to keep the weight off.[106] Using a more aggressive approach, they starved patients down to within 25% of ideal weight. At 18 months follow-up, 4 of the 12 who reached this goal had regained the lost weight, but 8 had maintained the weight loss although they "required constant supervision."[128] It is difficult to decide whether such dramatic starvation is more beneficial, or if we are only seeing an effect of what

Feinstein refers to as the physician's role as watchdog.[50]

Medical therapy simply does not have much to offer the obese patient. Certain groups have a better chance of being successful at a diet -- men, highly motivated patients, those with adult-onset obesity -- but results are not very predictable.[200] The problem is that "dieting doesn't cure, it must be continued forever."[3]

D. SURGERY

When medical management of obesity fails, a variety of surgical procedures can be employed. These include removal of local fat deposits, wiring the jaws shut, and major surgery.[108] Two gastric procedures have been well described: the gastric bypass, which is a 90% gastric exclusion with a retrocolic gastroenterostomy; and the gastroplasty, which divides the stomach into a small upper reservoir connected by a narrow channel to the bulk of the stomach. In both procedures the small gastric chamber leads to early satiety and a voluntary reduction in intake. Operative mortality is 2-5% and complications are few: chiefly stomal ulceration in the gastric bypass and obstruction in the gastroplasty. Weight loss averaged 100 pounds in the first year post-gastric bypass, according to one report.[155] Gastroplasty is somewhat less successful, and weight loss at one year averages about 50 pounds. The disadvantage of gastric surgery is that patients may learn to eat continuously, which completely nullifies the procedure. The gastric remnant or upper pouch often dilates, requiring revision.[155]

In more common use is the jejunoileostomy or intestinal bypass. There are variations, but all bypass the greater part of the small bowel by anastomosing the proximal jejunum to the terminal ileum. Payne preserves 14 inches of functional jejunum, which he anastomoses end-to-side to 4 inches of terminal ileum.[146] Scott uses 12 inches of jejunum and 6 inches of ileum, which he anastomoses end-to-end; the distal end of the bypassed bowel must be drained into the colon.[175] (See diagram p.61 .)

The jejunoileostomy works on the principle of malabsorption due to a limited surface area for absorption of foodstuffs. Despite virtually

unlimited intake, a person will not gain weight after a bypass.[108,175] Weight loss is usually rapid in the first 3 months, and then tapers until the weight reaches a plateau around 18 months post-operatively. Most patients lose from 80-120 pounds. Other benefits include a decrease in cholesterol levels, improvement in diabetes, and in many cases the normalization of hypertension.[13]

Because of a number of complications (particularly hepatic failure, but also electrolyte imbalance and intractable diarrhea, arthritis, and urinary tract stones), most surgeons have set strict criteria for the procedure. In general, jejunoileostomy is reserved for (1) the morbidly obese (twice ideal weight or 100 pounds over ideal weight for at least 5 years), (2) who have failed vigorous medical management, (3) in the absence of a correctable endocrinopathy, (4) and with complications of their obesity (hypertension, diabetes, Pickwickian syndrome, venous stasis, arthritis, inability to properly care for body hygiene), (5) who promise to avoid alcohol postoperatively.[52,148,217,27] Contraindications to the procedure include severe cardiovascular disease, recent pulmonary embolus, chronic liver failure, absent or incontinent anal sphincter, and acute psychiatric disorders (although Weismann states that a psychiatric diagnosis is rarely a contraindication).[217,20]

Internists have been extremely wary of the procedure, as are many surgeons. Nonetheless, it is estimated that 5,000 jejunoileostomies have been performed in the U.S.[20] A recent editorial gave reluctant approval to the operation if the above-mentioned stringent criteria are strictly applied, and even went so far as to approve the procedure for hospitals outside major teaching centers if an internist, surgeon, and psychiatrist worked together with each patient.[108]

The following is a report of a series of jejunoileostomies performed in an 11 bed hospital in rural Montana by a family practitioner who served the combined roles of surgeon, internist, and psychiatrist.

II. NINETY-THREE CASES OF JEJUNOILEOSTOMY: WEIGHT LOSS, CHANGES IN BLOOD PRESSURE, AND COMPLICATIONS

A. MATERIALS AND METHODS

Starting with the first jejunoileostomy in 1969, over 90 intestinal bypass procedures have been done at the Liberty County Hospital in Chester, Montana by Dr. R. S. Buker, Jr. Indications for surgery have been somewhat looser than the strict criteria employed in most studies in the current literature. The major requirement in this series was long-standing obesity with a failure of medical management to produce weight loss. The definition of obesity was a relative one, and involved a consideration of body weight, height, and ideal body weight as predicted by insurance company tables. Arbitrary figures such as weight greater than 100 pounds over ideal or weight twice ideal were not employed. Many patients had complications of their obesity (hypertension, diabetes, Pickwickian syndrome, arthritis, venous stasis), or had reached the point where they were unable to care for their own body hygiene. These were important factors in the decision to proceed with surgical therapy.

Surgical procedure. The operative procedure, identical in every instance, consisted of anastomosing ten (10) inches of jejunum, measured from the ligament of Treitz, to eight (8) inches of ileum, measured from the ileocecal valve, in an end-to-side manner (Figure 1). The distal end of jejunum was oversewn and then tacked down to the bowel to prevent intussusception. A few changes in technique were made after the first cases: (1)Because of a problem with herniation through the longitudinal incision, all further cases

were performed through a transverse incision above the umbilicus; (2) to reduce the number of operative complications and to shorten intra-operative time, appendectomies were not routinely performed; (3) the abdominal cavity was lavaged with a solution of 500 mg kanamycin suspended in 500 cc sterile saline to reduce the incidence of wound infections.

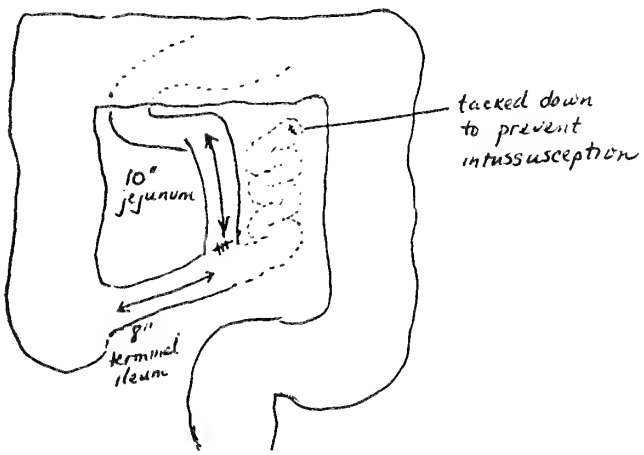

FIGURE 1. Surgical procedure

Patient population. All patients who underwent jejunoileostomy at the Liberty County Hospital from July, 1969 (the first procedure) through April, 1976, were included in this study. There were 93 such patients. Their ages ranged from 16 to 61 years. Fourteen were male and 79 female. Pre-operative weights ranged from 162 to 466 pounds (mean 263 $\pm$ 6). Patients were a mean of 104 $\pm$ 3% over ideal weight (range 45% to 231% over ideal weight).

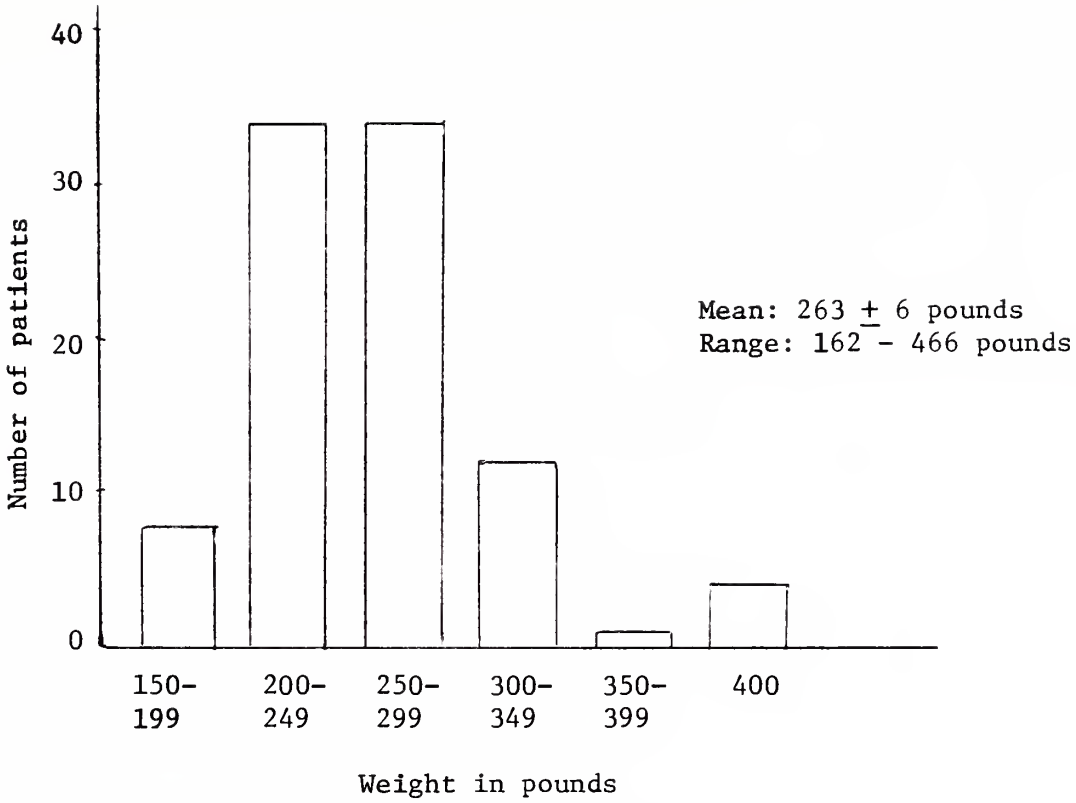

FIGURE 2. Weight prior to jejunoileostomy.

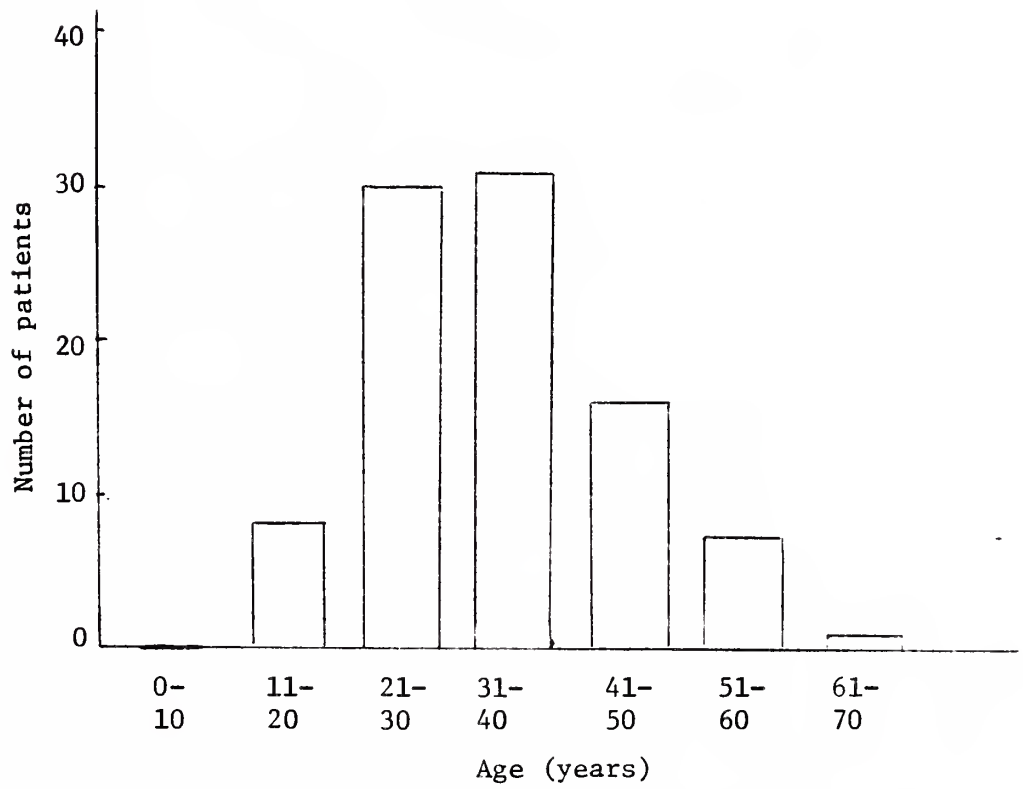

FIGURE 3. Age at jejunoileostomy.

Methods

(1) Chart review

A review of the outpatient chart, including discharge summary of each local hospitalization, of each of the 93 patients was undertaken to assess operative and post-operative complications and changes in blood pressure. Blood pressure and weight were recorded with each clinic visit (including an initial visit prior to surgery), with a few exceptions. Blood pressure was taken with the patient seated in the examining room, by an experienced nurse using a standard blood pressure cuff, before the patient was seen by a physician. In those cases in which the blood pressure measurement was repeated by the physician, the lower of the values was used for the purposes of this study. Hypertension was defined as systolic pressure exceeding 140 mm Hg or diastolic pressure exceeding 90 mm Hg. When a single borderline reading was available (e.g., 145/90), a patient was considered hypertensive if he or she reported a history of hypertension and if review of the in-hospital chart confirmed a consistent elevation in blood pressure. Weights recorded in the chart were taken with the patient ordinarily dressed, using an office (balance-beam) scale. These values were rounded to the nearest pound. Relative weight was defined as $\frac{\text{Patient's weight}}{\text{Ideal weight for height}} \times 100$. Ideal weight was derived from a standard Metropolitan Insurance Company Table, using the mean value for a "medium frame."

Using serial recordings of blood pressure, pre- and post-operative outpatient blood pressures were compared at follow-up of 3 weeks, 2-4 months, 6-12 months, and > 12 months. Patients taking anti-hypertensive medications were excluded from the analysis. Follow-up was available on a total of 62 patients, but because some

patients did not keep appointments the number of patients evaluated at each interval varied slightly. Using each patient as his own control, Student's paired t-test was applied to changes in systolic and diastolic pressures at each follow-up period. Student's t-test for independent means was used to compare the mean change in blood pressure between pre-operative normotensive and hypertensive patients. In a group of 21 patients who could be followed longitudinally, Student's paired t-test was used to assess the significance of changes in blood pressure from pre-operative levels and from blood pressure at 3 weeks post-operatively.

Pre- and post-operative blood pressures were also compared at different levels of absolute and relative weight loss. Again, patients on anti-hypertensive medication were excluded, and Student's paired t-test was used to evaluate the significance of the observed changes. Mean reduction in blood pressure among those who were normotensive pre-operatively was compared with mean reduction among those who were hypertensive prior to surgery at each level of weight loss, using Student's t-test for independent measures.

Despite patient education on the potential hazards of the surgery, outpatient follow-up was somewhat less than ideal. In several cases after one or two clinic visits, patients were lost to follow-up entirely. In other instances, because of the distance involved, patients saw their local physician for many health problems post-operatively, returning only infrequently to Dr. Buker for routine check-ups. Thus the occurrence of late complications as assessed by the chart review is probably an underestimation.

(2) Questionnaire

A questionnaire was sent to the 49 patients whose surgery had been performed at least 2 years prior to this study. The questionnaire (Appendix A) was designed to evaluate the following: (1) Current weight, (2) changes in work and marital status, (3) complications, and (4) patient satisfaction. Thirty of the 49 patients returned completed questionnaires; an additional 3 patients were interviewed but did not complete questionnaires; 3 patients had died; and 13 were lost to follow-up.

B. RESULTS

WEIGHT LOSS

In almost every case there was an early rapid weight loss associated with severe diarrhea. Figure 4 shows the mean weight of 32 subjects followed for 2 years after surgery. The rapid phase of weight loss ended by 4-6 months and weight stabilized around 18 months after jejunoileostomy.

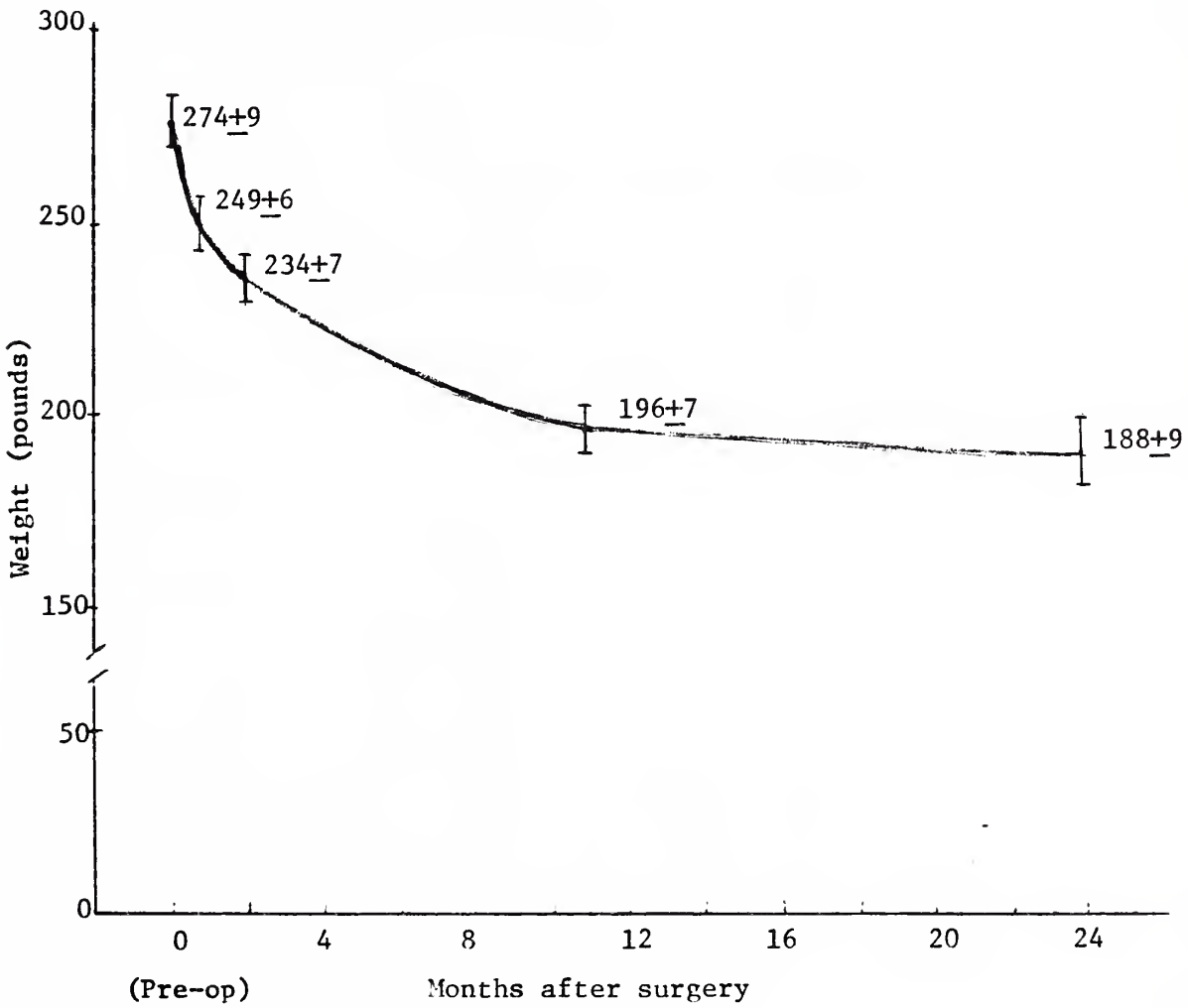

FIGURE 4. Mean weight in patients followed for 2 years (N = 32).

Information on weight at one year follow-up was available from the charts of 45 patients. Mean weight loss at one year was 79 ± 4 pounds (or 29 ± 1% of pre-operative weight). There was a significant correlation between pre-operative weight and weight loss at one year after surgery ($r = 0.70$, $P < 0.001$). Thus patients who weighed more prior to surgery could anticipate a greater absolute weight loss.

Current weight was reported by 29 patients who returned questionnaires and by 3 patients who were interviewed. Follow-up in all cases was at least 2 years and averaged 3 years, 5 months. In most cases weight had already stabilized by 18 months (Figure 4) and underwent only minor fluctuations thereafter. Pre-operative weights varied from 196 to 435 pounds in these 32 people. Current weight ranged from 115 to 296 pounds. Mean weight loss was 95 ± 6 pounds (or 34 ± 2% of pre-operative weight). From Figure 5 it can be seen that 6 of the 32 patients (19%) lost less than 70 pounds after jejunoileal bypass (weight loss in these patients was 39, 40, 40, 52, 53, and 55 pounds).

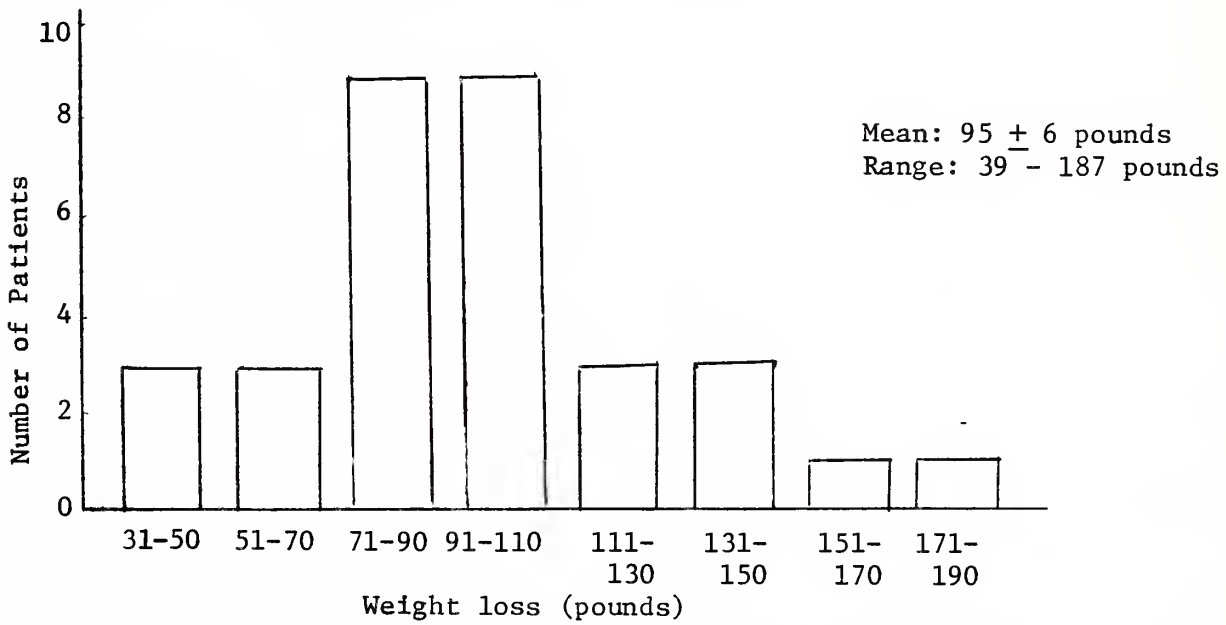

FIGURE 5. Reported weight loss in 32 jejunoileostomy patients on long-term follow-up.

Nineteen of 30 subjects reported on questionnaire or interview that their obesity had begun before puberty (Question: Before surgery, when was the last time your weight was "normal"?). Eight had obesity beginning after puberty, in "adult" life, and 3 did not reply to the question. Pre-operative weight was significantly different between these two groups: pre-pubertal obese weighed 290 $\pm$ 13 pounds and adult-onset obese weighed 246 $\pm$ 13 pounds prior to surgery ($P < 0.05$). Adult-onset obese patients came to surgery later in life (mean age 43 $\pm$ 4 years compared to 32 $\pm$ 3 years for pre-pubertal obese patients, $P < 0.05$). Post-operative weight loss did not differ significantly between the two groups.

Four patients out of the entire group of 93 underwent revision of the bypass surgery because of inadequate weight loss (4.3%). In the first case the patient lost only 8 pounds over the first 3 post-operative months. On re-exploration it was found that an additional loop of ileum had been included in the original anastomosis. When this was corrected the patient went on to lose weight satisfactorily (124 pounds at last follow-up, 4 years after surgery). In the other 3 cases weight loss was 39, 57, and 97 pounds (the latter in a woman who weighed 342 pounds prior to surgery). One of these patients was lost to follow-up; one had lost 17 pounds when last seen 3 weeks after revision; and the third was recuperating from the surgery at the time of this study. In each case at surgery hypertrophy and elongation of the remaining functional bowel was found.

One other case of problematic weight loss was a woman who began to gain weight 2 years, 8 months after bypass. Her weight has risen steadily since. Although she is at present 88 pounds lighter

than her pre-operative weight, her maximum weight loss was 119 pounds.

BLOOD PRESSURE

Relative weight and pre-operative blood pressure. A significant correlation was found between relative weight before surgery and both pre-operative systolic ($r = 0.52$, $P < 0.0001$) and diastolic ($r = 0.24$, $P < 0.05$) blood pressure. When the analysis was restricted to women (complete data was available on only 10 men) and broken down into groups according to age, the correlation was much less marked and in fact was not significant for diastolic pressure (Table 2). In young women the correlation persists for systolic pressure, but in women over 40 years relative weight is not significantly correlated with systolic blood pressure.

TABLE 2

Pre-operative blood pressure and relative weight in 64 women

Age	N	Mean Blood Pressure, mm	Mean Relative Weight	Correlation Coefficient	P
SYSTOLIC					
16-29	24	146 ± 5	205 ± 7	0.64	<0.0002
30-39	22	144 ± 5	204 ± 7	0.42	<0.05
40-59	18	161 ± 6	202 ± 5	0.32	NS
DIASTOLIC					
16-29	24	92 ± 3	205 ± 7	0.16	NS
30-39	22	90 ± 3	204 ± 7	0.33	NS
40-59	18	100 ± 3	202 ± 5	0.27	NS

Change in blood pressure after surgery. Changes in blood pressure after surgery in 62 patients not on anti-hypertensive medication are shown in Table 3. As was mentioned previously, the variation in the number of patients evaluated at each follow-up interval is due to failure of patients to keep routine appointments. Both systolic and diastolic blood pressure fell to a significantly greater degree in those patients who were hypertensive pre-operatively. Mean weight loss and mean follow-up time after surgery were not significantly different between pre-operative hypertensives and normotensives at 3 weeks, 2-4 months, and > 12 months. However at 6-12 months follow-up, hypertensives had lost a mean of 78.8 pounds over 9.9 months while normotensives lost a mean of 62.2 pounds over 8.3 months ($P < 0.05$ in both cases).

Table 3 suggests that there is an initial rapid fall in blood pressure post-jejunoileostomy, followed by a more gradual decrease over time. However a fairly large number of patients missed follow-up at one or more of the intervals used. A group of 21 patients were each seen at 3 weeks, 6-12 months, and > 12 months. Table 4 records the mean systolic and diastolic pressures in these patients as they were followed over time. Mean weight loss at each of the follow-up periods did not differ significantly between the normotensive and hypertensive groups. (See Appendix B for BP details).

Blood pressure fell significantly in both groups, except for diastolic pressure in the normotensive group. Hypertensives showed a greater drop in blood pressure at 3 weeks follow-up, but from this point on the two curves are parallel (Figure 6). When changes in blood pressure from the pressure noted at 3 weeks were compared between the

two groups at 6-12 months and > 12 months, there were no significant differences. After 3 weeks, both systolic and diastolic blood pressures in pre-operative normotensives and hypertensives changed to the same extent. Thus the greater overall reduction in blood pressure in pre-operative hypertensives appears to be entirely due to a larger early fall in blood pressure. This reduction was sufficient to produce a normal mean blood pressure (137.6/81.8) at follow-up of over 12 months.

TABLE 3

Mean change in blood pressure with time after surgery

	SYSTOLIC (mm Hg)		DIASTOLIC (mm Hg)	
Time post-op:	3 weeks		3 weeks	
All patients followed (47)	-13.6±2.6		-7.1±2.3	
Normal BP pre-op (16)	-5.5±3.1*	P<0.01	+0.5±2.7*	P<0.005
HBP pre-op (31)	-17.7±3.4		-10.7±3.0	
	2-4 months		2-4 months	
All patients followed (50)	-19.0±3.2		-10.2±2.4	
Normal BP pre-op (17)	-9.6±2.5	P<0.05	-6.1±3.4*	P-NS
HBP pre-op (33)	-23.9±4.4		-12.3±3.2	
	6-12 months		6-12 months	
All patients followed (38)	-21.6±4.7		-15.2±2.7	
Normal BP pre-op (8)	-9.8±2.8	P<0.02	-4.5±2.7*	P<0.0025
HBP pre-op (30)	-24.8±5.8		-18.1±3.1	
	12 months		12 months	
All patients followed (31)	-27.1±4.5		-18.7±2.9	
Normal BP pre-op (9)	-15.8±3.3	P<0.02	-11.8±4.3	P<0.05
HBP pre-op (22)	-31.7±6.0		-21.5±3.5	

* Not significantly different from zero by Student's paired t-test. All other values significantly different from zero ($P<0.05$).

TABLE 4

Longitudinal follow-up of blood pressure in
21 patients post-bypass surgery

Time	All patients (21)	P*	Normal BP pre-op (5)	P*	HBP pre-op (16)	P*
			MEAN SYSTOLIC BP ± S.E.M.			
Pre-op	160.5 ± 5.5		132.8 ± 3.3		169.1 ± 5.6	
Post-op: 3 weeks	143.5 ± 4.6	<0.005	126.0 ± 6.0	NS	149.0 ± 5.7	<0.005
6-12 months	144.3 ± 5.1	<0.005	124.4 ± 6.1	NS	150.5 ± 5.7	<0.005
12 months	133.1 ± 4.6	<0.005	118.8 ± 6.5	<0.05	137.6 ± 3.4	<0.005
			MEAN DIASTOLIC BP ± S.E.M.			
Pre-op	100.8 ± 3.5		84.4 ± 3.4		105.9 ± 3.6	
Post-op: 3 weeks	88.6 ± 3.0	<0.005	80.8 ± 2.4	NS	91.0 ± 3.7	<0.005
6-12 months	87.4 ± 3.0	<0.005	79.2 ± 5.5	NS	90.0 ± 3.9	<0.005
12 months	79.9 ± 2.9	<0.005	74.0 ± 5.9	NS	81.8 ± 3.3	<0.005

* P values for comparison with pre-operative BP, using Student's paired t-test.

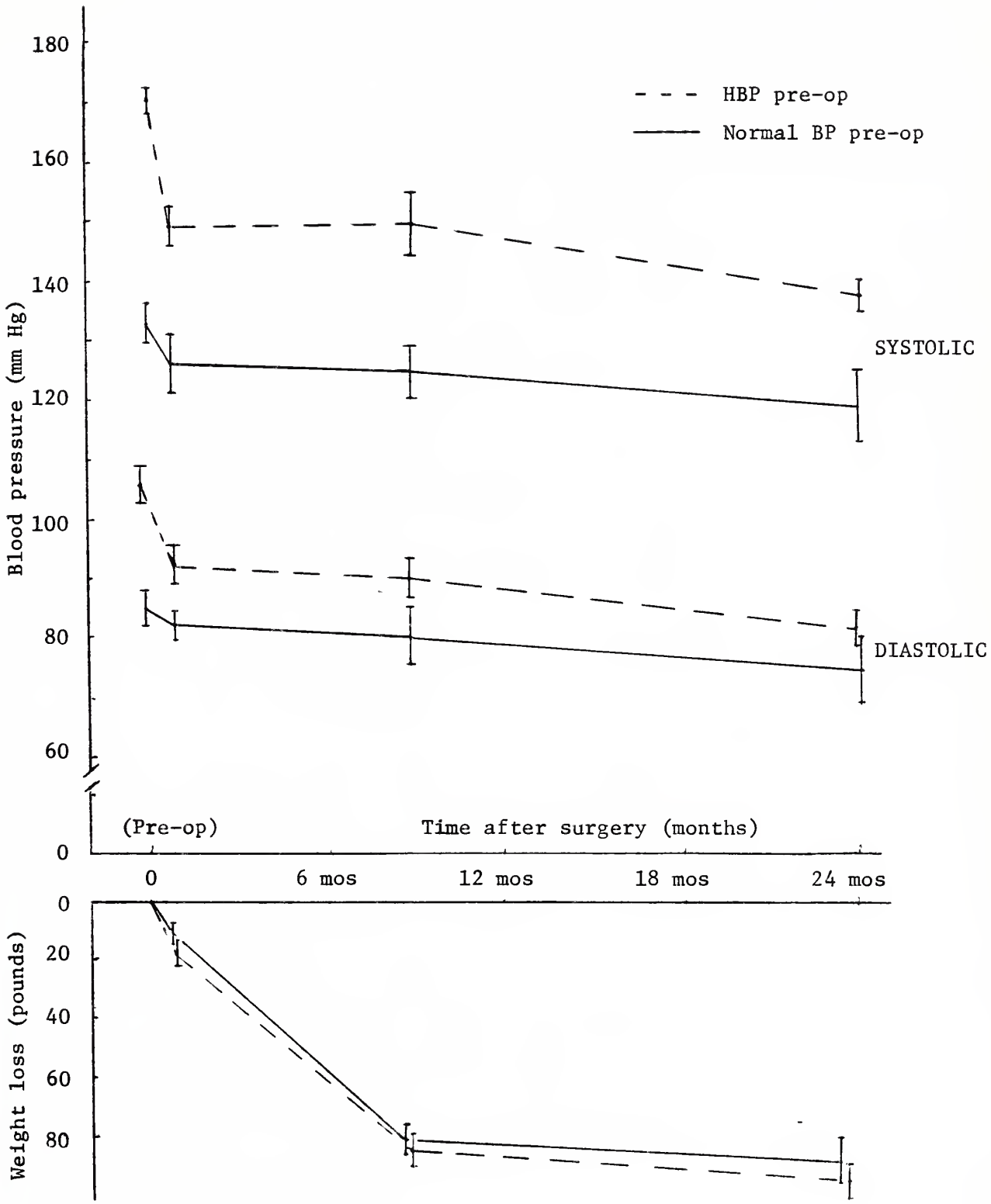

FIGURE 6. Blood pressure and weight loss in 21 patients followed longitudinally after jejunoileostomy (Mean $\pm$ S.E.M.).

Pre- and post-operative blood pressures were also compared at given levels of weight loss (Table 5). Except for values marked with an asterisk, change in blood pressure from pre-operative levels was statistically significant. Again pre-operative hypertensives showed a greater fall in blood pressure. Systolic pressure tended to fall more than diastolic.

Because pre-operative hypertensives were heavier before surgery than normotensives were (264 ± 7 compared to 229 ± 8 pounds, $P < 0.05$), change in blood pressure with weight loss was re-examined with weight loss expressed as a per cent of initial body weight (Table 6). The pattern is very similar to that in Table 5, with those who were hypertensive prior to surgery showing a significantly greater drop in blood pressure.

The number of patients who could be followed through all levels of weight loss (absolute or relative) was small and precluded a longitudinal analysis of change in blood pressure with progressive weight loss. However Tables 7 and 8 show that there is a significant positive correlation between weight loss (both absolute and relative) and change in both systolic and diastolic pressure in patients who were hypertensive before surgery. This analysis was done at a follow-up of greater than 12 months after surgery (mean 2.2 years), by which time weight has begun to stabilize. No relationship could be demonstrated between weight loss and change in blood pressure in those who were normotensive prior to surgery.

TABLE 5

Mean change in blood pressure with weight loss after surgery

	SYSTOLIC (mm Hg)	DIASTOLIC (mm Hg)
Weight Loss:	15-24 pounds	15-24 pounds
All patients followed (37)	-18.4±2.4	-9.9±2.4
Normal BP pre-op (14)	-13.1±3.3	-1.4±4.1*
	P<0.05	P<0.005
HBP pre-op (23)	-21.7±3.1	-15.0±2.5
	25-34 pounds	25-34 pounds
All patients followed (32)	-13.6±3.4	-3.3±2.5*
Normal BP pre-op (12)	-2.8±3.0*	+0.1±3.3*
	P<0.005	P-NS
HBP pre-op (20)	-20.1±4.7	-5.2±3.5*
	35-54 pounds	35-54 pounds
All patients followed (32)	-18.0±4.9	-8.3±2.9
Normal BP pre-op (11)	-7.1±2.4	-1.6±4.0*
	P<0.05	P<0.05
HBP pre-op (21)	-23.7±7.0	-11.8±3.7
	≥55 pounds	≥55 pounds
All patients followed (29)	-19.4±3.5	-15.8±2.6
Normal BP pre-op (8)	-6.3±4.0*	-3.0±2.0*
	P<0.005	P<0.005
HBP pre-op (21)	-24.5±4.2	-20.7±2.8

* Not significantly different from zero by Student's paired t-test. All other values significantly different from zero (P<0.05).

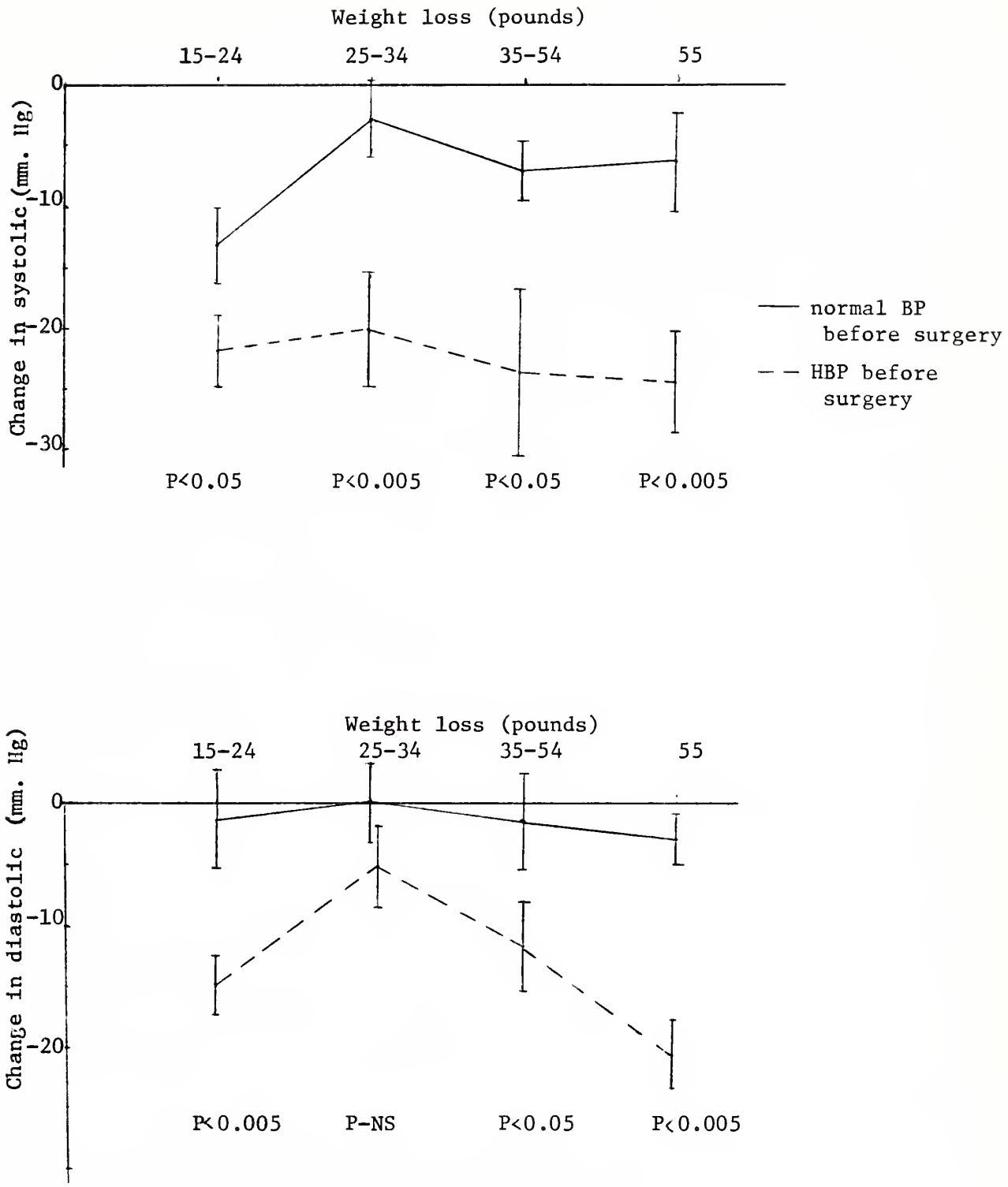

FIGURE 7. Change in blood pressure with weight loss after surgery (Mean $\pm$ S.E.M.).

TABLE 6

Mean change in blood pressure with weight loss
(% initial weight) after surgery

Weight loss (% initial weight):	SYSTOLIC (mm Hg)	DIASTOLIC (mm Hg)
	≤9.9%	≤9.9%
All patients followed (51)	-16.0±2.6	-10.0±2.2
Normal BP pre-op (18)	-8.2±3.1	-2.6±3.2*
	P<0.01	P<0.005
HBP pre-op (33)	-19.7±3.4	-14.1±2.6
	10.0-19.9%	10.0-19.9%
All patients followed (46)	-14.1±3.6	-4.1±2.3*
Normal BP pre-op (18)	-6.0±2.6	-0.5±2.6*
	P<0.05	P-NS
HBP pre-op (28)	-19.4±5.5	-6.4±3.3
	20.0%	20.0%
All patients followed (35)	-19.1±3.0	-15.2±2.3
Normal BP pre-op (12)	-8.0±2.9	-4.7±2.9*
	P<0.005	P<0.005
HBP pre-op (23)	-24.9±3.8	-20.7±2.6

* Not significantly different from zero by Student's paired t-test. All other values significantly different from zero (P 0.05).

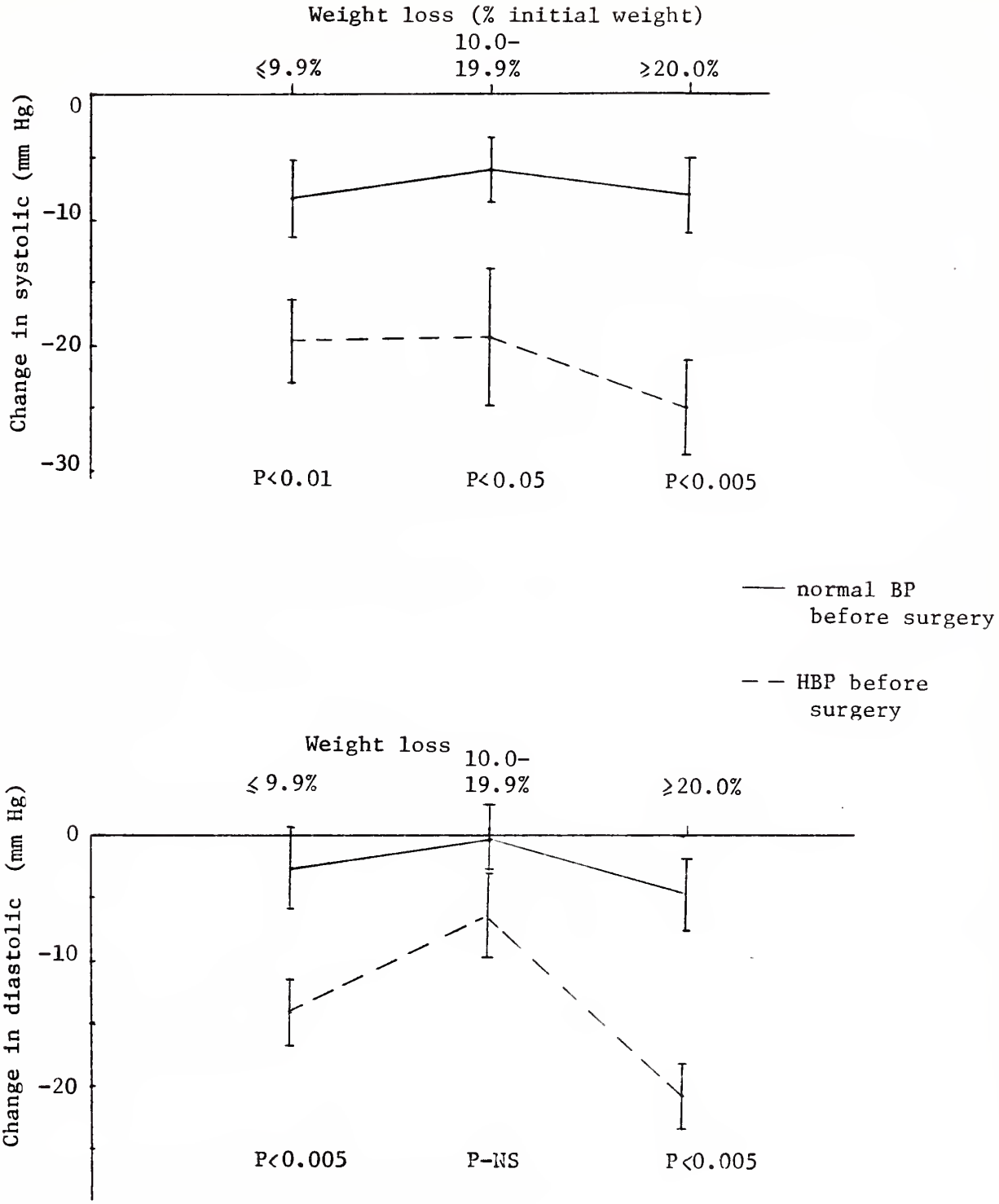

FIGURE 8. Change in blood pressure with weight loss (% initial weight) after surgery (Mean ± S.E.M.).

TABLE 7

Correlation between absolute weight loss and change in blood pressure at > 12 months follow-up (mean = 2.2 years)

	Change in systolic BP	Change in diastolic BP
All patients followed (31)	r = 0.62	r = 0.45
Normal BP pre-op (9)	-0.15*	-0.23*
HBP pre-op (22)	0.68	0.55

* Not significantly different from zero.
All other correlation coefficients significant ($P < 0.005$).

TABLE 8

Correlation between relative weight loss and change in blood pressure at > 12 months follow-up (mean = 2.2 years)

	Change in systolic BP	Change in diastolic BP
All patients followed (31)	r = 0.46	r = 0.34
Normal BP pre-op (9)	0.16*	0.02*
HBP pre-op (22)	0.59	0.48

* Not significantly different from zero.
All other correlation coefficients significant ($P < 0.05$).

Reversion of hypertension to normal. Of the 49 patients whose surgery was performed at least 2 years prior to this study, 34 were found to be hypertensive pre-operatively. Three of these 34 subsequently died, and 3 others were lost to follow-up. As the remaining 28 hypertensives were followed after bypass, the number demonstrating normal blood pressure ($< 140/90$) progressively increased. At 8 months after surgery 50% had become normotensive, and 18 (64%) were normotensive at final follow-up (Figure 9). Mean pre-operative systolic and diastolic blood pressures and mean relative weight did not differ significantly between the group that remained hypertensive and the group that became normotensive after surgery (Table 9). Nor could the two groups be distinguished by pre-operative weight or post-operative weight loss. Age at surgery, however, was lower in the group who subsequently became normotensive (33 ± 3 years compared to 42 ± 3 years, $P < 0.05$).

TABLE 9
Comparison of pre-operative parameters

	Mean Systolic BP	Mean Diastolic BP	Mean Relative Weight
HBP normalized post-op	172 ± 6 mm	106 ± 4 mm	218 ± 7
HBP persisted post-op	176 ± 9	107 ± 3	222 ± 15

Since weight loss increases with time post-operatively, the relationship between weight loss and normalization of blood pressure was examined. Column 1 of Table 10 gives the weight loss at which normal blood pressure was first noted in each of those who subsequently remained normotensive. Figure 10 is a graph of the per cent normotensive against weight loss.

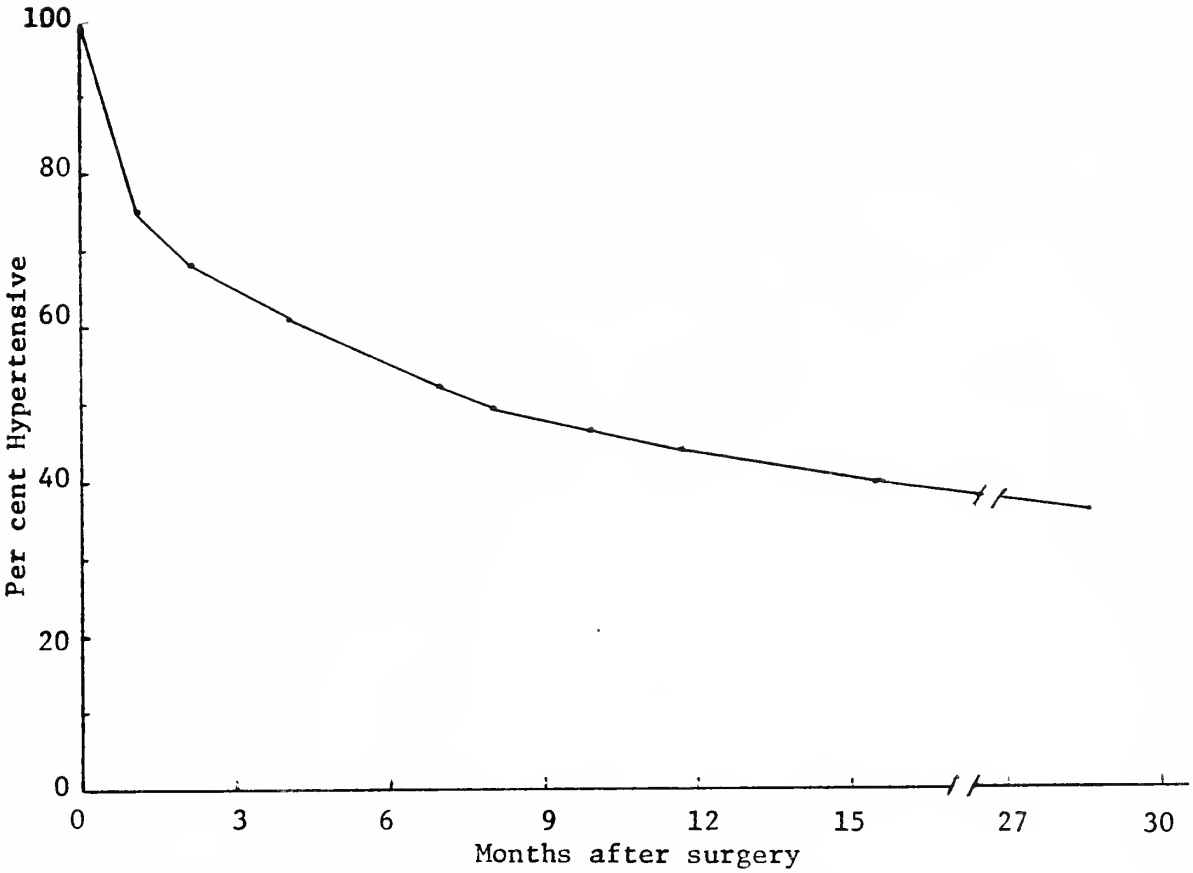

FIGURE 9. Per cent of pre-operative hypertensives (N=28) remaining hypertensive on long-term follow-up.

TABLE 10
Weight loss and blood pressure in 28 hypertensives

Weight loss (pounds)*	Number Normotensive	Cumulative Normotensives	Per Cent Normotensive
0	0	0	0
15	2	2	7
22	1	3	11
23	1	4	14
27	1	5	18
30	1	6	21.5
38	1	7	25
43	1	8	28.5
49	2	10	35.5
57	1	11	39
78	1	12	43
83	1	13	46.5
89	1	14	50
92	1	15	53.5
96	1	16	57
108	1	17	61
179	1	18	64

* Weight loss achieved at the time BP first noted to be normal and after which no further hypertensive levels were recorded.

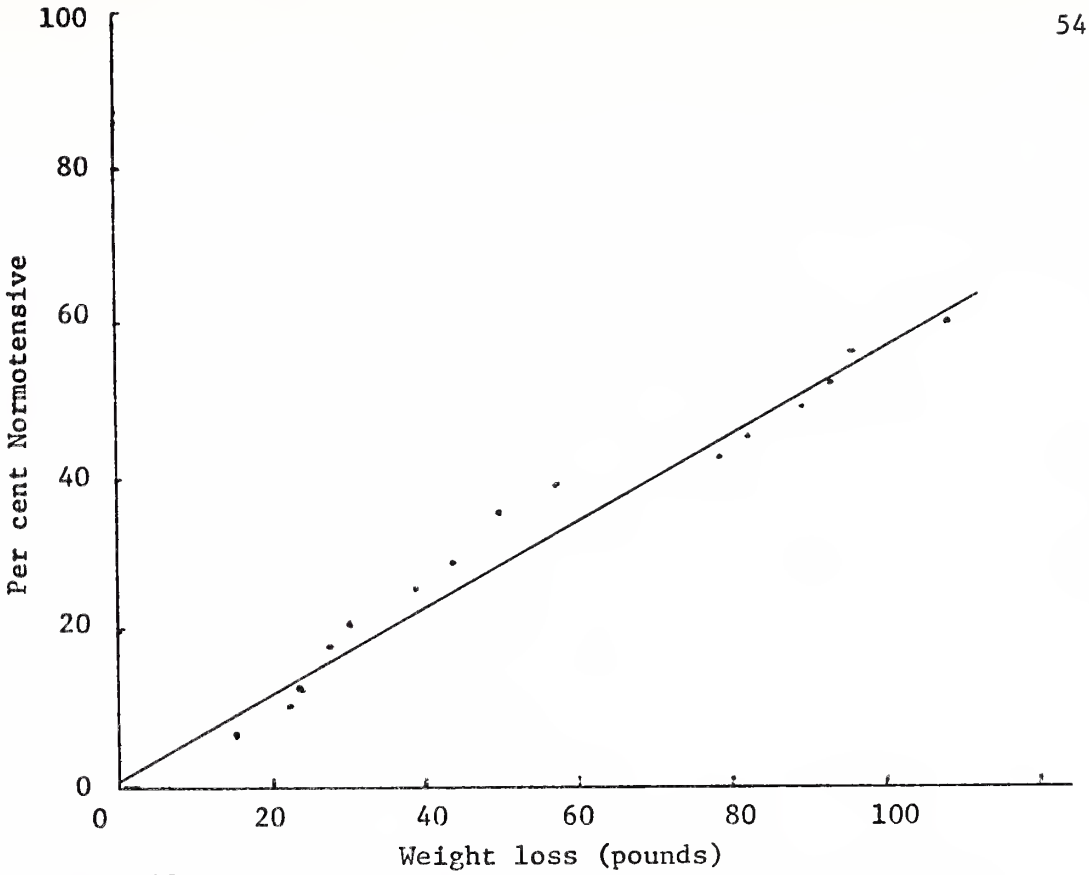

FIGURE 10. Weight loss and normalization of blood pressure in 28 hypertensive patients.

An increasing percentage of pre-operative hypertensives became normotensive with increasing weight loss up to 100 pounds. Very few patients lost more than this amount of weight, and the effect of further weight loss on blood pressure cannot be predicted.

SOCIAL

Marriage and children. Marital status in 32 patients at least two years after bypass surgery was reported as follows: 18 married, 6 single, 7 divorced, and 1 separated. Five of the marriages, three divorces, and the single separation occurred after jejunoileostomy.

Two women had children after surgery. This was the second child for one of them. The other woman was a 19 year old who was nulliparous at the time of surgery.

Work. A total of 8 of the 29 patients who completed questionnaires stated that they had been on Welfare at some time. Five patients were Welfare recipients pre-operatively. After surgery 3 of these 5 no longer received Welfare benefits; however an additional 3 patients went onto Welfare after surgery. Thus the number of patients on Welfare pre- and post-operatively was identical.

Job status was assessed from the questionnaire. Most patients did not report their salaries, so that changes in employment cited below refer to full versus part-time work or unemployment. Twenty-two patients resumed their former level of employment after surgery (only one of them remained unemployed to a degree unexplained by age, physical disability, or household duties). Another 5 patients actually worked more after surgery, moving either from unemployment to a part or full-time job, or from part-time to full-time employment. Finally 2 patients were working less after surgery than before. One of these was "not able to hold a job, since I get ill and I am not able to function properly." This woman was on Welfare at the time of follow-up. A second woman, who was 20 years old, was only working part-time, although she had worked full-time for the first post-operative year.

COMPLICATIONS

Mortality. There have been a total of 4 deaths out of the group of 93 patients (4.3%). One was related to a technical error, i.e., the bowel was perforated by a misplaced clamp. Clinically this patient became hypotensive on the second post-operative day, passed

bright red blood per rectum, and despite transfusions died before re-exploration was possible. The other 3 deaths occurred suddenly, within one month of surgery. H.S., a 60 year old insulin-dependent diabetic with hypertension, developed dyspnea and a cough post-operatively, which led to wound dehiscence. After operative repair he became increasingly dyspneic and cyanotic and suffered a cardiac arrest on the fifth post-operative day. E.J., a 61 year old with hypertension and a history of thrombophlebitis, required oxygen post-operatively to keep her P_{O_2} within a reasonable range. She was able to progress rapidly to a regular diet, however, and was discharged on the eighth post-operative day. She died suddenly at home several days later. B.W., a 466 pound hypertensive, underwent re-exploration for a malfunctioning bypass on the eighth post-operative day; the anastomosis had been improperly formed and was revised. He developed a wound infection and then hepatitis, but recovered uneventfully, only to die suddenly one month after the original procedure. No autopsy material was available on any of the last three cases; clinically death was attributed to pulmonary embolization or myocardial infarction.

Morbidity. Short and long term complications among the 93 subjects are recorded in Table 11. This data was derived from the chart review and supplemented where appropriate with information from the questionnaires. Because a number of patients did not return for routine follow-up, complications have probably been underestimated.

Four of the 93 bypasses performed were revised because of inadequate weight loss, as mentioned previously. A single patient had her bypass taken down. She stated that she had been terribly

sick for a year, requiring hospitalization for "kidney trouble." On the advice of her personal physician she had the bypass reconnected at another hospital.

Patients responding to the questionnaire reported a number of symptoms after jejunoileostomy. Most of these were gastrointestinal, but there were also frequent complaints of dizziness, weakness, and muscle cramps. Half the subjects noticed hair loss after the surgery. Three patients stated that they had been bothered by gallstones post-operatively, and two reported anemia (undocumented).

TABLE 11
COMPLICATIONS IN 93 PATIENTS POST-JEJUNOILEOSTOMY

Wound infections	6	(6.4%)
Hepatitis	2*	(2.1%)
Metabolic (Hypokalemia or hypocalcemia requiring in-hospital treatment)	2	(2.1%)
Urinary tract stones	3+	(3.2%)
Obstruction 2^{o} adhesions	1#	(1%)
Abdominal pain, unknown etiology	2	(2.1%)
Acute colonic distension	1	(1%)
Ventral hernia	7≠	(7.5%)

* One patient died suddenly after recovering from hepatitis
\+ One CaPO4 (negative for oxalate); one reported as Ca; one not retrieved.
\# Node at exploration revealed regional enteritis.
≠ 2/7 were recurrences.

TABLE 12
SYMPTOMS REPORTED BY 30 PATIENTS AFTER BYPASS SURGERY

Diarrhea	27	(90%)	Muscle cramps	7	(23%)
Bloating	22	(73%)	Joint pains	6	(20%)
Abdominal cramps	14	(47%)	Dizziness	9	(30%)
Vomiting	5	(17%)	Weak spells	8	(27%)
			Hair loss	15	(50%)

In response to the question, "Have you been under a doctor's care for any medical problems since your operation?", the following were reported:

TABLE 13
MEDICAL PROBLEMS SINCE SURGERY IN 30 PATIENTS

Diabetes	1	(3%)	Thyroid	2*	(7%)
Kidney stone	2	(7%)	Gallbladder	1	(3%)
Hernia/ lipectomy	3	(10%)	Fluid retention	2	(7%)
Electrolytes	1	(3%)	Gout/ arthritis	3	(10%)
Phlebitis	1	(3%)	Other	4#	(13%)
Ob/Gyn	7	(23%)			

* one thyroidectomy; one thyroiditis.
# automobile accident, UTI, "stomach trouble," unspecified renal disease.

Twelve of the 30 patients denied taking any medications on a daily basis. Ten took vitamins and/or minerals daily; 2 were taking calcium and 3 potassium; 4 were using diuretics. A few other drugs were mentioned as being used regularly, including "Mylicon" and "Colbenemid."

PATIENT SATISFACTION

When asked, "If you had to do it all over again, would you have this operation for your weight problem?", replies were as follows: 23 Definitely yes, 3 Probably yes, 3 Probably no, and 1 Definitely no. There was no trend in terms of weight loss or the number of complications noted on the questionnaire. The single patient who had her anastomosis taken down answered the question with

"probably no." In general patients were ecstatic about the weight loss and enthusiastic about the surgery. Appendix C contains excerpts from the comments made by subjects completing the questionnaire.

III. DISCUSSION

JEJUNOILEOSTOMY

A. BENEFITS

On the basis of studies in dogs, Kremen was the first to suggest that obesity might be treated by "removing from intestinal continuity sufficient small bowel to produce weight loss without any other serious hazard or impairment."[100] He actually performed a jejunoileostomy for this purpose almost 10 years before Payne's first jejunocolic shunt. Payne abandoned the jejunocolic shunt because of severe metabolic complications and high mortality. Part of his original study design was to take down the anastomosis once a satisfactory weight was reached. In early cases he discovered that the weight was quickly regained. This led him to revise the jejunocolic shunt to a jejunoileal anastomosis. He found that weight was regained with as little as 35 inches of bowel in functional continuity.[147] Thus he adopted a more radical bypass, anastomosing 14 inches of jejunum end-to-side to 4 inches of ileum. This procedure preserved the ileocecal valve and the bile acid and B_{12} absorptive surface of the terminal ileum.[146,148,171] Scott, citing inadequate weight loss due to reflux of intestinal contents into the bypassed loop of bowel, began a trial of the end-to-end bypass. He retained 12 inches of both jejunum and ileum, later reducing the length of ileum to 6 inches. The distal end of the bypassed bowel was drained into the colon.[173] These are the two basic types of jejunoileostomy, on which individual surgeons have imposed minor variations.

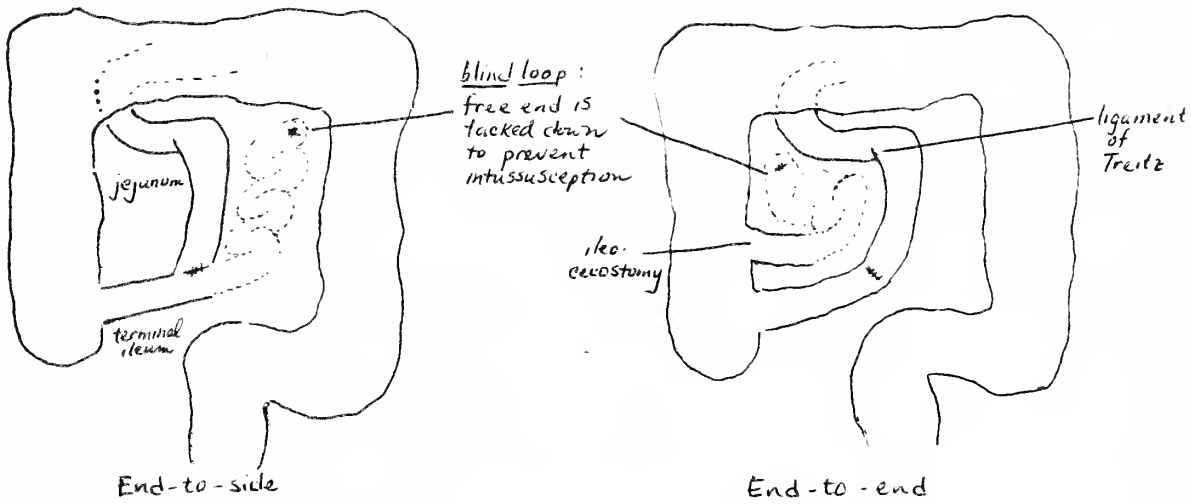

FIGURE 11. End-to-side and end-to-end variations of jejunoileostomy.

WEIGHT LOSS

In terms of weight loss, the critical factor is the length of functioning intestine. If over 25 inches of intestine are left in continuity, weight loss will be slow.[20,108] Scott and others have found a faster weight loss in those with shorter anastomoses.[175,217] Although malabsorption is a major factor in producing weight loss, caloric restriction is also important. Because eating exacerbates diarrhea and indigestion, many patients voluntarily limit their intake.[127]

There is an early phase of rapid weight loss that lasts 1-3 weeks. This corresponds to about 10% of the pre-operative weight and is thought to be largely body water.[72] A second phase of constant weight loss follows. Salmon demonstrated a significant correlation between the rate of weight loss and initial weight.[165] Others have found the duration of weight loss to be dependent on initial weight.[72] As in previous

reports[69], initial weight in this study correlated with weight loss at one year ($r = 0.70$, $p < 0.001$). Basal metabolic rate increases with increasing obesity[15], and since absorption is fixed by the bypass procedure, those who are heavier will have a greater caloric deficit and will lose more weight.

Absolute weight loss varies from individual to individual and from series to series (Table 14). It is surprising that detailed information on initial weight and weight loss is not available in more of the case reports in the literature. Payne reports a mean weight loss of 97 pounds at one year and 110 pounds at two years after 14+4 end-to-side bypass. Average pre-operative weight was 308 pounds.[148] Benfield's patients had lost a mean of 96 pounds after 6 months. Pre-operative weight in this group averaged 348 pounds.[20] In the present study weight loss was somewhat less impressive, averaging 79 pounds at one year follow-up and 95 pounds at follow-up of over two years. (The latter figure if anything overestimates weight loss, since it is derived from the current weight reported by 32 subjects. No information is available on weights of patients who did not respond to the questionnaire.) However patients in this series weighed considerably less than those in either of the above groups. Average pre-operative weight of all 93 patients was 263 pounds, and the 49 patients followed for over 2 years weighed a mean of 280 pounds. Since weight loss after surgery is correlated with initial weight, it appears that this would account for the discrepancy.

In general, weight loss continues for 12-18 months before leveling off. Buchwald found that 90% of his patients came within 50 pounds of ideal weight.[28] Two-thirds of Salmon's patients (also end-to-end anastomoses) came within 20 pounds of ideal weight by 1-3 years after

TABLE 14

Type of jejunoileostomy and weight loss

Series	Procedure end-end	Procedure end-side	N	Mean initial weight (pounds)	Mean weight loss (pounds)
Scott[175]	12+12* 12+ 6		12 50	(240-486)	No data
Salmon[165]	10+20		120	(180-390)	No data
Buchwald[28]	16+1.6		94	290	33% below pre-op (?time)
Fikri[52]	14+ 4		52	(110-240 over ideal)	95 (1 year) 130 (2 years)
Weismann[217]		15+5† 14+4	133	(50->200 over ideal)	101 (>1 year) 130 (>1 year)
Jewell[87]	10+10 10+12	15+5 14+4	52	314 (e-e)⊛ 294 (e-s)	No data
Payne[148]		14+4 15+5	140	308	97 (1 year) 110 (2 years)
Benfield[20]	16+ 4	16+4	30	348	96 (6 months) 156 (2 years)
Starkloff[191]	12+ 8	14+4	475	(>125 over ideal)	103 (>1 year, e-s)
PRESENT SERIES		10+8	93	263±6	79±4 (1 year) 95±6 (>2 years)

* 12+12 refers to 12 inches jejunum anastomosed to 12 inches terminal ileum.

⊛ "e-e" stands for "end-to-end" and "e-s" for "end-to-side" .

† A number of other combinations were used in this study in small numbers.

surgery.[165] Weight stabilizes because of adaptation of the bowel. The functioning segment becomes hyperplastic, elongates, and dilates, presenting a larger surface area for absorption.[173] None of Payne's original 58 patients plateaued at a weight below ideal.[146] However at times weight does not even approach ideal. Inadequate weight loss (defined by Jewell as less than 5 pounds/month/year[87] and by Starkloff as stabilization at a level more than 50 pounds over "anticipated normal weight"[191]) occurs in up to 15% of cases.[108] In this series, 19% of 32 patients had lost less than 70 pounds on long-term follow-up. However 2 of these 6 patients were within 50 pounds of ideal weight. Inadequate weight loss in patients with end-to-side bypasses is primarily due to reflux into the bypassed segment of bowel.[146,156] The incidence of inadequate weight loss is much lower in end-to-end anastomoses: neither Scott nor Buchwald reported weight loss under 80 pounds; Salmon mentions only 2 cases in his series of 120 in which the procedure was a failure in terms of weight loss.[175,28,165] (It should be noted that Salmon left 30 inches of bowel in continuity, which is more than the length recommended for optimal weight loss.) When faced with poor weight loss, many surgeons will revise or shorten the bypass. Incidence of such revisions, performed only for inadequate weight loss, is shown in Table 15.

Anywhere from 4 to 10% of end-to-side procedures are revised for inadequate weight loss. In the present series a comparable number of revisions were performed (4.4%). Revision is only rarely required for end-to-end bypass, except when a lengthy segment of bowel is left in continuity.

One patient in the Montana series was beginning to regain weight 2

TABLE 15
BYPASS REVISIONS FOR INADEQUATE WEIGHT LOSS

END-TO-END	REVISIONS	(%)	END-TO-SIDE	REVISIONS	(%)
Scott(175)	0/ 62		Payne(148)	16/165+	(9.7%)
Salmon(165)	2/113*	(1.8%)	Weismann(217)	5/123x	(4%)
Jewell(87)	1/ 17‡	(6%)	Benfield(20)	2/ 30	(6.7%)
Buchwald(28)	0/ 94		Starkloff(191)	13/273	(5%)

* 10+20 revised to 10+10
‡ in a 12+12 end-to-end jejunoileostomy
\+ 12 underwent resection of elongated bowel; 4 were changed from end-to-side to end-to-end.
x an additional 2 referred from another hospital underwent revision.

years, 8 months after bypass. She may have developed reflux or extensive adaptation of the functioning bowel. As adaptation occurs, GI distress diminishes and patients may increase their intake. Fikri has reported a similar weight gain of 15-30 pounds in 3 of his 52 patients several years after end-to-end bypass.[52] The incidence of such late malfunction of the jejunoileostomy is not known, and the question of whether the weight loss induced by jejunoileostomy is permanent is a valid one.

HYPERTENSION

As was mentioned previously, hypertension is more common in the obese. In the Framingham study only a modest correlation was found between relative weight and systolic blood pressure ($r = 0.3$).[91] A somewhat larger correlation was demonstrated in this series of obese subjects ($r = 0.52$). Differences between the populations involved were important, since the Framingham Study consisted of a large adult population while the present group is composed of the extremely obese,

particularly obese women. Since the Framingham Study showed that both blood pressure and weight increase with age in women[91], the correlation coefficient was recalculated grouping women subjects by age. A smaller correlation was noted, which was only significant in the age 16-29 and 30-39 groups. It would seem then that relative weight is more important with regard to systolic blood pressure in women under 40; from 40 on, age and other factors may play a larger role.

Weight loss has a favorable effect on blood pressure [35,99,112,117,140,154] (Table 16). This was noted already in 1923 when Preble followed 194 subjects who were overweight and found that both systolic and diastolic pressures fell with weight loss. He did not separate his group into normotensives and hypertensives, but in a separate study he suggested that fall in BP is more dramatic in severe hypertensives.[154] Similarly Terry's study of obese women with hypertension showed a drop in blood pressure with weight loss.[206] Martin compared changes in blood pressure in obese normotensives and hypertensives who lost weight. Although obese normotensives lost more weight, blood pressure fell to a greater degree in obese hypertensives. Martin did not consider a change in blood pressure significant unless the systolic changed by at least 20 mm. Hg or the diastolic by 15 mm. Hg. He concluded that weight loss exerted a minor effect on blood pressure, although on the average systolic pressure fell by almost 16 points in his obese hypertensives.[112]

Fletcher's careful study of changes in blood pressure in obese hypertensive and normotensive women on a weight-reducing diet is particularly pertinent to this report. He defined systolic hypertension as a systolic pressure over 150 mm. Hg, and diastolic hypertension as a diastolic pressure over 90. Systolic blood pressure fell by a mean of 32.8 mm. in women

TABLE 16

Influence of weight loss on blood pressure in obese subjects

Reference	Characteristics	Mean Weight	Mean BP (mm Hg)	Mean Weight Loss (pounds)	Mean Change Systolic BP	Mean Change Diastolic BP
Preble[154] 1923	194 subjects ≥ 10 pounds over ideal	No data	155/96	≥10	-21	-10
	62 subjects ≥ 10 pounds over ideal	No data	219/129	≥10	-43	-21
Terry[206] 1923	24 obese women with HBP	approximately 200	196/103	12 (?)	-26	-8
Master and Oppenheimer[117] 1929	53 obese subjects	No data	No data	25-30	-25-30	-15-20
Salzano[166] 1958	16 obese subjects (2/16 systolic >140)	194	126/73	41	-13	-9
Martin[112] 1952	19 obese subjects with HBP	212.6	178/99	35.7	-15.8	-4.8
	18 obese subjects with normal BP	218.8	139/77	42.3	-7.9	-2.8
Fletcher[53] 1954	38 obese women with HBP	(45% over ideal)	196/116	32.4	-32.8	-16.5
	21 obese women with HBP	(48% over ideal)	184/110	4.2	+0.5	+1.3
	12 obese women with normal BP	(44% over ideal)	134/88	30	-10.8	-3.5

with systolic hypertension who lost an average of 32 pounds, and by 10.8 mm. in normotensive women who lost a mean of 30 pounds. Women with systolic hypertension who did not lose weight had essentially no change in systolic pressure. Similarly, diastolic blood pressure fell by a mean of 16.5 mm. in women with diastolic hypertension who lost an average of 33 pounds, and by 3.5 mm. in normotensive women who lost an average of 30 pounds. Again hypertensive women who did not lose weight showed no change in diastolic pressure. Arm girth decreased by a mean of 3.5 cm. $\pm$ 1.8 cm. (s.d.) in a combined group of hypertensive and normotensive women who lost weight. Separate figures for each subgroup were not reported. Fletcher suggested that the fall in blood pressure in normotensive women who lost weight was due to a change in arm girth and that hypertensive women who lost weight experienced a true fall in blood pressure over and above the error due to arm girth.[53]

Reports of change in blood pressure following intestinal bypass surgery have been much less elaborate, but it is clear that blood pressure in hypertensives falls after bypass. Fikri found that 11 of 20 hypertensives became normotensive post-operatively, and an additional 8 experienced an improvement in their hypertension.[52] All 8 of Payne's hypertensive patients who underwent jejunocolic shunts became normotensive on follow-up.[147] Seventy-five per cent of Buchwald's 94 cases had hypertension pre-op (systolic > 140 and/or diastolic > 90). After bypass he states that "nearly all had a significant decrease in blood pressure" and "many became normotensive."[28] None of these studies has reported longitudinal follow-up of blood pressure, nor have they considered changes in blood pressure at different levels of weight loss post-op. Emphasis has been on blood pressure changes in the hypertensive patient, without

mention of changes in normotensive subjects.

The current study demonstrates that blood pressure falls significantly in both hypertensive and normotensive patients after 10+8 end-to-side jejunoileostomy for morbid obesity. Both systolic and diastolic blood pressure fell to a greater degree in patients who were hypertensive prior to surgery than in those who were normotensive. A marked early decline in blood pressure in hypertensives appears to account for the entire difference. Weight loss at 3 weeks (the bulk of which is fluid[72]) averaged only 17 pounds in hypertensive subjects. After 3 weeks blood pressure continued to decline gradually and to the same degree in pre-operative hypertensives and normotensives (Figure 6).

Dahl postulated that a decreased sodium intake, rather then weight loss per se, was responsible for the early reduction in blood pressure in obese hypertensives on low calorie diets. He hypothesized that obese hypertensives were more sensitive to sodium ingestion and restriction than were lean hypertensives.[41] The results of the present study suggest the possibility that obese hypertensives might be more sensitive to changes in fluid and/or salt balance than obese normotensives. Although the difference in blood pressure changes between obese hypertensives and normotensives has been noted before in patients losing weight by dieting[53,112], it has not previously been suggested that this is due to a larger early fall in blood pressure in hypertensives. Earlier studies have not examined longitudinal changes in blood pressure. Rather they have compared blood pressure before and after a given time interval or degree of weight loss. Thus these investigations may not have detected the rapid early fall in blood pressure that was seen in the present series. It is not known

whether the more gradual, late change in blood pressure observed in this study is mediated through a prolonged effect of volume and sodium depletion on the baroreceptors or through some effect induced by weight loss or the bypass surgery itself.[19,183]

When pre-operative hypertensives and normotensives were examined at different levels of weight loss (either expressed in absolute terms or as a per cent of initial weight), hypertensives again showed a greater fall in systolic and diastolic blood pressure. There appeared to be a tendency for blood pressure in pre-op hypertensives to fall further with increasing weight loss (Tables 5 and 6). However composition of the groups at different levels of weight loss differed slightly. Since it was not possible to follow a sufficiently large group of patients longitudinally, one cannot definitely conclude that blood pressure declines directly with increasing weight loss after surgery. However the data suggest a relationship, since on long-term follow-up a significant correlation was found between weight loss (both absolute and relative) and change in blood pressure in the hypertensive group. These figures were quite similar to the correlation coefficients Fletcher found in obese hypertensive and normotensive women who lost weight.[53] In the present study no correlation could be demonstrated between weight loss and change in blood pressure in pre-operative normotensives.

When the group of pre-op hypertensives was studied in detail, it was found that 18/28 (64%) became normotensive on long-term follow-up. Three of the 10 who remained hypertensive showed improvement in their blood pressure. Weight loss was not significantly different between those who remained hypertensive and those who became normotensive, nor did the two groups differ in several other pre-operative parameters. However mean

age of the group whose blood pressure reverted to normal was almost ten years lower than the mean age of subjects whose hypertension persisted. It may be that older patients had hypertension of longer duration that was more resistant to changes occurring after bypass. Or it is conceivable that there are different subtypes of hypertension in obese subjects. Because a number of hypertensive patients became normotensive within a few months of surgery, the effect of weight loss was examined (Table 10). A linear regression was fitted to the data graphed in Figure 10, and the following formula was derived:

$$Y = 2.0 + 0.56\ X$$

where X = weight loss in pounds, $0 \leq X \leq 108$
Y = % normotensive at weight loss of X pounds

According to this equation, half of those who were hypertensive pre-op would be normotensive on reaching a weight loss of 85 pounds. A weight loss of 175 pounds satisfies the equation for Y = 100%. However extrapolation beyond a weight loss of 90-100 pounds is not accurate because of the small number of patients who achieved this degree of weight loss. It is impossible to predict what effect further weight loss would have on blood pressure, particularly since age seems to play a role.

Blood pressure readings in this study were drawn from the outpatient charts of obese subjects. All had been taken by an experienced nurse, and the proportion of readings ending in an integer other than 0 or 5 suggests that they were recorded with care. It was not possible to average several BP readings at each visit, since BP was often taken only once. When 2 values were recorded during the same outpatient visit, the lower one was used for the purposes of this study. Subjects with borderline blood pressure readings were considered hypertensive only if

they reported a history of hypertension and if the hospital chart confirmed a consistent elevation of blood pressure. Both of these methods would tend to place hypertensive patients in the normotensive category.

Two extraneous factors could have been elevating the pre-operative blood pressure: (1) tension surrounding the up-coming surgery; and (2) a "cuff artifact." The tension factor cannot be excluded by the available data, since blood pressure readings weeks or even months before surgery were not recorded. However, the differences between hypertensives and normotensives cannot be explained by anxiety unless one postulates that hypertensives are more responsive to stress. Although weight loss may be unmasking a cuff artifact as Fletcher suggests[53], blood pressure fell before sufficient weight loss had occurred to affect arm girth. Furthermore, cuff artifact cannot explain the greater early fall in blood pressure seen in pre-operative hypertensives. It is possible that the gradual late change in blood pressure observed in this study in both hypertensive and normotensive patients was due to the unmasking of such a cuff artifact. Some studies have shown a spontaneous fall in the blood pressure of hypertensives over lengthy follow-up (6-9 years), and it is conceivable that this contributed to late changes in blood pressure in the present study.[76,192]

OTHER MEDICAL BENEFITS

Jejunoileostomy has a beneficial effect on other risk factors associated with obesity. The following is a brief summary of the changes seen in cholesterol, triglycerides, and glucose intolerance following bypass surgery, although data in the present series did not include these factors.

Buchwald was among the first to note that patients who underwent major ileal resection (ileal bypass) had a decrease in plasma cholesterol.[25] This procedure is slightly different from the jejunoileostomy -- specifically, the terminal ileum is excluded -- but the basic principles leading to a lowered cholesterol apply to both procedures. Not only is less cholesterol absorbed (absorption takes place preferentially through the distal small bowel), but interference with the enterohepatic circulation leads to an increased production of bile acids from cholesterol in the liver, thereby increasing cholesterol turnover. Triglyceride levels also fall, partly because of changes in carbohydrate intake.[27] In all studied patients post-jejunoileostomy, both cholesterol and triglycerides have decreased significantly. In one report cholesterol declined by 40% and triglycerides by 50%.[28] Ten of 12 patients with Type IV hyperlipidemia in Scott's series had normal lipid profiles after bypass.[175] Because the literature is consistent on this point, cholesterol and triglycerides were not routinely measured before and after bypass in the present study. As the risk of coronary heart disease increases exponentially with rising cholesterol, a lowered cholesterol may be of benefit.[173]

The insulin resistance and glucose intolerance of the obese has already been mentioned. After bypass, the glucose tolerance test tends to normalize.[175,217] More importantly, frank diabetes becomes easier to control. Of Fikri's 5 diabetics, 2 no longer required medication and 3 needed less insulin post-operatively.[52] Buchwald reports similar findings.[28] This has been attributed to diminished glucose absorption[146]; however, the role of increased insulin sensitivity associated with loss of adipose tissue is probably of greater importance.[48]

PSYCHOSOCIAL

As discussed previously, there are no distinctive behavioral abnormalities associated with obesity other than overeating. Dieters experience a remarkable number of symptoms --weakness, "nervousness," nausea-- most of which are attributed to oral deprivation and the stress of continually resisting temptation.[186] Stunkard has described a more serious depressive syndrome.[196] In the light of these findings it is important to assess the psychological changes in patients post-jejunoileostomy. Solow, in a major evaluation of 29 patients, found a significant improvement in depression, self-esteem, and body cathexis post-bypass. Patients were more active, reported interpersonal relationships as more satisfying, and demonstrated increased self-assertiveness. Six of his 29 patients had some type of psychiatric illness during follow-up, which he related to previous psychiatric problems. He found that the degree of weight loss was related to decrease in depression and improved ego strength.[186]

Most investigators have not been able to document any substitute symptoms appearing with weight reduction in these patients, but several have noted an increase in "emotionality," with more anxiety, depression, and irritability.[20] One psychiatrist reported that 40 of the 65 patients he was following required psychotherapy for "anxiety and depression."[32] Scott states that depression is common in the early post-operative months.[175] Both Bray and Solow noted a decrease in denial after weight loss, which they thought was important in terms of the number of symptoms reported.[20,186] In the current series, very few emotional problems were observed post-bypass. Patients were generally very pleased with the change in their life-style. In interviews several confided that they felt like different

people, and that this had placed some stress on old dependent relationships.

Another psychological change seen after intestinal bypass is reversal of the body image distortion.[20,186] This is most notable in attitudes toward others: "A recurrent theme among bypass patients was increasing reluctance to mingle with fat people."[32] Similarly, in the present series one woman being interviewed stated flatly, "I cannot stand fat people." Another wondered why they (obese people) didn't cover up more.

Most reports of jejunoileostomy have included a short statement to the effect that most (if not all) patients returned to their former constructive employment or became employable because of the weight loss.[165,175] Buchwald found that the rate of "gainful employment" increased in his series of patients after weight reduction.[28] One editorial states "...the procedure appears to have a good record for rehabilitation of these unfortunate people back to a useful active life."[202] Some states have even been willing to pay for jejunoileostomy because of its success in getting patients off Welfare.

The present study casts some doubt on the role of jejunoileostomy in economic rehabilitation. Although work records are difficult to quantitate, it was found that employment did not change drastically after weight loss. The number of subjects on Welfare before and after surgery remained the same. The jejunoileostomy patients had a remarkably poor record of paying their hospital bills compared to other surgical patients at Liberty County Hospital. One woman received her insurance company's check and promptly spent it on a new wardrobe.

It is possible that the economic situation across the country has prevented a complete "rehabilitation" of these people. However it is

equally likely that the Montana series, which was much less selective than reports in the literature, contained a larger proportion of the unmotivated and/or unemployable. That this is true to some extent (with regard to motivation) can be seen from the poor follow-up record of most of these patients, despite emphasis on the importance of periodic check-ups and the seriousness of complications. This has important implications in terms of a broad application of the jejunoileostomy: motivation is critical if adequate follow-up and appropriate management of complications is to be achieved.

B. EARLY COMPLICATIONS

Mortality. Mortality rate (bypass-related) in large reported series varies from 0.7% to 8%. In reviewing 989 bypass procedures, Bray found 42 deaths either within 1 month of surgery (any cause) or any time thereafter (directly related to surgery), an incidence of 4%. The most frequent cause of death was liver failure, followed closely by pulmonary embolism and surgical (technical) problems.[20] The operative mortality of 4.4% in the present series compares favorably with these figures. It is important to emphasize that this surgery was performed in a small hospital; anesthesia was administered by a nurse-anesthetist; and no volume respirator was available for those with post-operative respiratory insufficiency. Patients were encouraged to ambulate in the first 24 hours (in many, use of a bedpan was impossible, and early ambulation was a necessity).

Wound infections. Wound infections are reported in various manners: "seromas" or serous drainage, "superficial" wound infection, dehiscence, evisceration. Incidence of all wound infections has ranged from 3.3% to 35%.[20] Serous drainage makes up a large proportion of this figure. The incidence of wound infections in the present series (6.4%) corresponds to that reported elsewhere. Dehiscence occurred in 2 patients, one of whom later died. Since wound infections occur in the early post-operative period, all these patients were seen at the Liberty County Hospital and this figure can be considered very accurate.

Diarrhea. Virtually 100% of bypass patients have diarrhea for the first few months post-operatively. One must suspect an inadequate bypass in those who do not. Severity of the diarrhea varies from 6 to 30 liquid

to semi-liquid bowel movements per day, and is exacerbated by excessive liquid or fat intake and by binge eating.[28] Transit time is rapid in the early post-operative months, and steatorrhea develops, but even the combination of these two factors is not sufficient to account for the degree of diarrhea seen. Because water and electrolyte loss may be greater than intake[103], it is postulated that some compound is irritating the colonic mucosa, leading to a net secretion. Free fatty acids (soaps) or bile acids could produce such an effect.

Because of the rapid transit time and malabsorption in bypass patients, free fatty acids pass unabsorbed into the large intestine. Fatty acids have been shown to increase colonic secretion, possibly because of their detergent action on cell membranes. Post-bypass patients with diarrhea have been treated with $CaCO_3$ on the hypothesis that precipitation with calcium would decrease fatty acid availability.[103] Their diarrhea does improve -- stools become pasty or semi-solid. However it is not clear that this improvement can be attributed to precipitation of fatty acids, since the glycine conjugates of bile acids are also bound by calcium.[79] Bile acids (regardless of the state of conjugation) are known to cause a reversible secretion of water and electrolytes into the lumen of the colon in the absence of any morphological damage. Hofmann and Poley demonstrated that a resin such as cholestyramine could decrease diarrhea in many patients after ileal resection. They postulated that resin binding of bile acids was the underlying mechanism.[79] At present it has not been determined whether fatty acids or bile acids do in fact contribute to the excessive diarrhea.

Most patients require narcotics to control diarrhea for the first few months after surgery, but the dose can be tapered and eventually

discontinued.[13,217] Experience has shown that a bland, fat-free diet avoiding raw vegetables and roughage is also helpful. Patients are advised to take small amounts of liquids frequently. Careful perianal skin care is important, as hemorrhoids and fissures occur commonly and may be difficult to manage.[191] In Salmon's series 25% had diarrhea at the end of the first year after surgery and only 13% after 2 to 3 years.[165] In the present series, 28/30 patients reported that diarrhea had been a problem; 14 said that even 2 years after surgery they still had episodes of diarrhea, often related to certain foods. However only one of these patients reported the need for an anti-motility agent.

Metabolic. The severity of metabolic changes after surgery generally parallels the severity of the diarrhea. Most cases of electrolyte imbalance can be managed on an outpatient basis with careful follow-up. The incidence of electrolyte imbalance requiring hospitalization is anywhere from 0 to 23% in reported series.[20] Only 2 instances of severe electrolyte imbalance are known to have occurred in this study (2.1%), but follow-up was incomplete.

Hypokalemia is the most frequently encountered problem. Starkloff noted this in 28% of his 300 patients.[191] Three of Scott's patients with 12+6 bypasses required oral potassium supplementation for months.[175] Hypocalcemia is also common. Calcium precipitates in the gut with unabsorbed anions, particularly fatty acids. Vitamin D deficiency secondary to malabsorption and hypomagnesemia may underlie or exacerbate hypocalcemia.[88] Routine supplementation with calcium and potassium does not necessarily prevent severe complications. One 36 year old woman died of hypocalcemia 8 months post-bypass, despite calcium supplementation when her symptoms first appeared.[44]

The immediate complications of electrolyte imbalance are serious enough, but no one really knows what the long-term effects may be. Decreased calcium absorption with a negative calcium balance can be expected to produce osteomalacia, although this has not yet been reported. Depleted stores of potassium and magnesium may result in renal complications over a long period of time.[146] Data simply is not yet available to assess these and other possible consequences.

Other metabolic complications include vitamin deficiency, hypoproteinemia, and anemia. Potentially, any vitamin deficiency may develop after jejunoileostomy.[87] Becuase of steatorrhea, fat soluble vitamins are especially likely to be malabsorbed. Scott showed that levels of vitamins A and E fall after bypass. In addition he found a prolonged prothrombin time in several patients during the early post-operative months, suggesting a deficiency of vitamin K.[175] Vitamin D malabsorption may also occur, leading to hypocalcemia.[88]

Hypoproteinemia and anemia may develop from malabsorption. Amino acid patterns are typical of malnutrition for the first 3 to 4 months after surgery.[126] In general this reverses, but on occasion severe wasting and edema develop. When hypoproteinemia is extreme re-anastomosis is indicated. Evidence of a milder, chronic protein malnutrition is suggested by changes in hair growth. Patients frequently complain of hair loss after bypass surgery. Buchwald et al reported this complication in 5 of 140 patients. Examination of hair follicles revealed a deficiency of keratin.[28] In the present series, 15 of 30 subjects who answered the questionnaire reported significant hair loss. Several reported that their hair was still thin and fine in texture two years after surgery.

Hyperuricemia has been observed after bypass surgery, but clinical

gout is uncommon (2% of Starkloff's 350 patients).[191] Both Scott and Weismann reported that uric acid levels rose during the first post-operative month, only gradually returning to pre-operative levels.[175,217] Weismann also noted a starvation ketosis in the early post-op period before a full diet was tolerated.[217] Competition of ketoacids with uric acid for renal tubular reabsorption may underlie the hyperuricemia.[19,101]

C. LATE COMPLICATIONS

Liver failure. An increase in fatty infiltration of the liver with occasional rapid progression to complete liver failure is the complication of most concern post-jejunoileostomy. It has been responsible for the greatest number of deaths. The exact frequency of this complication is difficult to determine accurately, for reasons which will become apparent.

Fatty liver is commonly present in the obese. Various series of intraoperative biopsies on jejunoileostomy patients report fatty infiltration in 60-100%, almost always without other pathological changes and frequently in the face of normal liver function tests.[26,146,202] Follow-up biopsies after surgery show that fatty infiltration increases in most patients. Fatty infiltration becomes particularly prominent during the first 6 months after surgery, when weight loss is rapid.[165] When symptoms occur, they tend to be gastrointestinal, e.g., nausea, vomiting, abdominal pain. The liver may be large and tender.[151] Most patients recover spontaneously, and biopsies over a year after surgery ordinarily show a decrease in fatty infiltration.[202] However progressive changes develop in 3-5% of patients. These patients present clinically with weakness and lethargy. Liver function tests usually reveal nonspecific changes; often, in fact, they remain normal until late in the course. Although the BSP retention is sensitive and may lead to early suspicion of an abnormality, it cannot be relied upon. Technetium liver scans show a diffuse decrease in uptake compared to pre-operative scans, which may be helpful in diagnosis.[81] Serial biopsies remain the best way of following the condition.[19] Early biopsies show an increase in

centrilobular fat. Fatty vacuoles may completely replace hepatocytes. Portal fibrosis and focal periportal necrosis develop. Bile duct proliferation and micronodular cirrhosis appear later. The terminal picture may be indistinguishable from alcoholic cirrhosis.[20]

The incidence of severe and fatal liver disease is reviewed in Table 17. Two cases of hepatitis occurred in the Montana series, one of which was followed by sudden death (attributed to a pulmonary embolus). The incidence of liver disease in this series is probably underestimated because of the number of patients lost to follow-up.

TABLE 17
Liver Disease Post-Jejunoileostomy

Series	Non-fatal liver disease(%)		Deaths, liver failure(%)	
Scott (175)	2/ 30	(6.6%)	0/ 30	
Salmon (165)	1/120	(1%)	0/120	
Buchwald (28)	2/ 94	(2%)*	0/ 94	
Fikri (52)	0/ 52		1/ 52	(2%)
Weismann (217)	2/123	(1.6%)+	1/123	(0.8%)
Jewell (87)	0/ 52		0/ 52	
Payne (148)	0/165		4/165	(2.4%)
Benfield (20)	0/ 30		1/ 30	(3.3%)
Starkloff (191)	3/475	(0.6%)	4/475	(0.8%)

* one reanastomosed; one treated with feeding jejunostomy into bypassed loop.
\+ attributed to drug or anesthesia

Although liver failure ordinarily develops in the first year after bypass, it has become clear that it is not related to either the rate or degree of weight loss, despite early reports to the contrary.[20] Perhaps the most convincing evidence in this regard comes from serial biopsies in patients who lost weight by dieting or fasting. Pre- and post-fast liver biopsies were compared in 10 patients who lost an average of 90 pounds over 71 days. Post-fast liver biopsies showed a marked decrease

in fatty infiltration. In a group of 7 patients who lost an average of 131 pounds over 5 months by dieting, even more complete regression of the fatty infiltration was noted. Long-term follow-up (average 17 months) in 14 subjects from both groups revealed essentially normal biopsies in 9, with minor (borderline) abnormalities in 5.[47] Rozental's study of 5 fasting patients confirms the above data. Even during starvation, 3 of the 5 had demonstrably less fatty infiltration.[163]

Theories to explain the progressive liver failure focus on either a nutritional deficiency or a toxin. It has been shown that in the first 3-4 months after bypass patients have amino acid levels typical of malnutrition (low fasting levels of most amino acids except for glycine and serine, which may be elevated). With weight stabilization these abnormalities reverse themselves.[126] Although the protein deficiency of kwashiorkor is associated with a prominent fatty infiltration of the liver, one cannot conclude that protein deficiency is responsible for fatty liver in bypass patients. In fact, there is evidence that liver function post-bypass may improve despite continued protein depletion, and may deteriorate even with adequate protein nutrition via hyperalimentation.[20] Other nutritional deficiencies are postulated, including vitamin E, essential fatty acids, and choline[102], but none of these has been linked directly to the liver failure seen post-jejunoileostomy.

Toxic substances may be responsible for liver damage after bypass. Lithocholic acid, which causes cirrhosis in a number of mammals, is a secondary bile acid resulting from bacterial action on chenodeoxycholic acid.[31] Ordinarily the primary bile acids are reabsorbed in the terminal ileum and recycled by the enterohepatic circulation. Primary bile acids that escape intestinal absorption are available for bacterial deconjugation

in the colon, and their end-products like lithocholic acid can be absorbed. Moxley found a level of lithocholate 14 times normal in the serum of a patient with post-bypass liver disease.[126] However lithocholate levels from bypass patients without liver disease are not available for comparison. The lithocholate hypothesis is not supported by the fact that patients undergoing ileal bypass for hyperlipidemia, in contrast to those with jejunoileostomy, do not develop liver failure.[28] Alcohol has been suspected in liver disease post-bypass, but thorough investigation has shown cases of liver failure in the absence of alcohol intake. At present there is no evidence that alcohol, either endogenous[122] or exogenous, plays a major role in liver failure post-jejunoileostomy. Patients are, however, advised to avoid alcohol post-op in order not to burden the liver with a known toxin. Recent work by O'Leary et al has focused attention on another possible liver toxin: bacterial endotoxin. These investigators performed 24+12 end-to-side bypasses in 8 dogs. Four received 100 mg. of Vibramycin daily in addition to a balanced diet, while the 4 controls received only a balanced diet. All 4 of the control dogs died of progressive fatty metamorphosis of the liver within 4 months of bypass. Bacteroides species and/or B. fragilis was cultured from the small bowel. The 4 experimental dogs had no liver abnormalities and grew no anaerobic organisms. O'Leary postulates that a bacterial endotoxin released from colonization of the defunctionalized loop of bowel may cause liver failure.[134] This data does not exclude the lithocholate hypothesis, as the antibiotic may rid the bowel of organisms that deconjugate and convert primary to secondary bile acids.

Therapy for post-bypass liver disease is non-specific: correction of nutritional deficits, cholestyramine, amino acid supplementation,

antibiotics, hyperalimentation. Results have been mixed. Reanastomosis is indicated in the face of progressive liver disease, but even this may come too late to save some patients.[19,20,126] It is the risk of liver failure which has turned many physicians away from the jejunoileostomy.

Urolithiasis. Kidney stones are a relatively common complication of jejunoileostomy. Reported incidence ranges from 5 to 15%.[20,45] In the present series three patients are known to have developed kidney stones (3.2%). Two consisted of calcium (one of these was negative for oxalate) and the third was not retrieved. This figure is probably low because of incomplete follow-up. Stones post-bypass commonly consist of calcium oxalate; in most cases patients with stones have hyperoxaluria, with normal serum calcium, phosphate, and uric acid and a normal 24 hour urine calcium.[52] Increased oxalate absorption is responsible for the hyperoxaluria. Since oxalate is absorbed by passive diffusion, solubility is an important factor. Binder's in vitro studies show that calcium chloride reduces oxalate solubility; when oleate is added, oxalate solubility increases.[11] In patients with steatorrhea, calcium binds preferentially to the abundant fatty acids (like the oleate in vitro) and more oxalate is available for absorption. Dehydration secondary to diarrhea is another major factor leading to urolithiasis. Therapeutically a low oxalate diet (avoiding tea, fruit juices, cocoa, beets, spinach) and liberal fluid intake are indicated. Calcium administration may be helpful. Cholestyramine decreases oxalate solubility in vitro, but has not yet been successful in clinical trials.[11,133]

Increased oxalate excretion in the absence of stone formation may cause renal damage. Vainder and Kelly report a patient who developed renal tubular acidosis (distal) seven years after bypass. Twenty-four

hour urinary oxalate was elevated and oxalate crystals could be demonstrated on renal biopsy.[209] A second patient, also with elevated 24 hour oxalate excretion, developed renal insufficiency 2 years after bypass. Biopsy showed interstitial nephritis and calcium oxalate deposition. The latter can be a nonspecific finding in uremia[40], but the evidence is highly suggestive that oxalate may produce serious renal complications years after jejunoileostomy.

Other GI complications. A number of gastrointestinal complications in addition to diarrhea and liver failure have been reported. Intussusception is currently a rare complication because the operative procedure includes anchoring the blind loop to the mesentery or the bowel itself. Internal herniation through mesenteric defects and volvulus have both been reported.[74] Obstruction may arise secondary to adhesions, as occurred in one patient in the present series. Ventral or incisional hernias are common. In the current series 5 were repaired; 2 recurred and required surgery a second time.

Passaro described a syndrome of "bypass enteritis" occurring 2 to 20 weeks post-operatively. It is characterized by an abrupt increase in diarrhea, with abdominal pain, distension, and fever. Diagnosis may be difficult, and patients have gone to laparotomy for presumed peritonitis or obstruction. Operative findings are inflammation, dilatation, and edema of the bowel. Pneumatosis cystoides of the defunctionalized segment is common.[145] The pathophysiology of this syndrome has not been entirely explained, but it is thought to be inflammatory in nature. If the diagnosis is considered, laparotomy may be avoided, since patients respond to antibiotics. Short-term antibiotics also relieve symptoms of bloating and gas associated with bacterial overgrowth of the defunctionalized limb

(blind loop syndrome).[108]

Reports of the "development" of gallstones post-bypass are difficult to interpret, since an oral cholecystogram is not a part of the routine pre-op work-up. Sorrell et al report 3 cases of acute pancreatitis due to stone impaction: in all three cases, the gallbladder was normal to palpation at bypass.[187] Potentially, the cholesterol:lecithin+bile salt ratio may be upset by the large losses of bile salts that occur post-bypass.[129,223] However, Buchwald states that in 140 cases he has not seen any instance of gallstones developing after surgery.[28]

Megacolon has occurred after jejunoileostomy, particularly in patients undergoing end-to-end anastomosis. Fikri reported 3 cases in his series of 52.[52] One patient in the present study was treated for this complication at another hospital. The area of dilatation of the colon is related to the point at which the defunctionalized loop of bowel drains: everything distal to that point will be affected. In an end-to-side procedure, this means the entire colon; in an end-to-end bypass it generally means the transverse, descending, and sigmoid colon. The blind loop contents have been blamed for this condition. Large numbers of obligate anaerobes can be cultured from the vicinity of the defunctionalized limb. (Colonic dilatation or pseudo-obstruction is also seen in other diseases associated with bacterial overgrowth, such as scleroderma and jejunal diverticulosis.) Treatment is primarily surgical because resistance to antimicrobial agents develops quickly.[20]

Mason and Printen report a patient who developed celiac sprue after bypass. Her symptoms did not improve with reanastomosis, but she did respond to a gluten-free diet. These authors suggest that jejunoileostomy might produce mucosal atrophy in the bypassed segment of bowel; if

this occurs, these patients could be predisposed to intestinal lymphoma or cancer. They suggest that atrophic small bowel mucosa be a strong indication for reanastomosis.[114]

Arthritis. A tenosynovitis and symmetrical polyarthritis has been described after intestinal bypass surgery. It occurs in about 10% of patients. In response to the questionnaire, 6 of 30 patients reported "joint pains" and 2 more had seen their doctor for "gout". One patient described stiffness of her hands and arms which appeared in the first few months after surgery and resolved gradually with physical therapy. Shagrin reported on 7 patients with jejunocolic bypass who developed arthritis. The wrist was affected in all 7 cases, the fingers in 5, and the knees and ankles in 3 each. Lab parameters, including RF, ANA, LE prep, creatinine, uric acid, calcium, phosphate, alkaline phosphatase, and cholesterol were entirely normal. He was able to control symptoms in 5 with rest and aspirin, but one patient required reanastomosis and another was still on steroids at the time of his publication. The patient who was eventually reanastomosed had a remission of her symptoms while treated with a course of tetracycline for a concurrent infection.[179] Buchwald noted 2 cases of polyarthritis in 140 end-to-end jejunoileostomies. When these patients discontinued the use of diphenoxylate for diarrhea, the symptoms abated. He suggested that a drug reaction was responsible.[28] However an equally reasonable explanation might be that the drug-induced decrease in motility had encouraged bacterial overgrowth. More recently, circulating cryoglobulin complexes containing IgG, IgM, IgA, C3, C4, and C5 were isolated from the serum of 3 patients with arthritis post-bypass. IgG against E. coli and B. fragilis was identified in the cryoglobulins. Two of the 3 patients had serum containing early

factors in the alternate activation pathway of complement. Both these factors and the cryoglobulin complexes disappeared when the arthritis resolved. Wands and his colleagues theorize that bacterial overgrowth occurs in the defunctionalized loop of bowel and that bacterial antigens reach the systemic circulation. Here cryoglobulin antigen-antibody complexes are formed that fix complement, activating it by either the classic or alternate pathway. These cryoglobulins are thought to play a key role in the pathophysiology of the arthritis.[212]

Miscellaneous. Brief mention should be made of a few other potential problems. It has been found that drug absorption is unpredictable post-bypass. The birth control pill must be considered an unreliable means of contraception in this population. Particular care must also be taken in the use of the coumadin/warfarin family of drugs.[13]

The small intestine is an immune organ, and one must ask what effects the bypass procedure will have on the body's defenses. Intestinal antibodies ("copro-antibodies") are known to protect animals from cholera, while circulating antibodies will not.[57] Studies of Peyer's patches have suggested that they are an important interface between antigens in the intestinal lumen and the body's lymphocytes.[144] Several cases of primary and reactivation TB have been reported after bypass.[7,152] The increased incidence of TB post-gastrectomy, although unexplained, has been recognized for many years; it is not known whether a parallel situation exists after jejunoileostomy or whether the state of protein depletion or some other factor plays the key role.

The long-term effects of such a drastic reorganization of anatomy are only now becoming apparent and will gradually be recognized and explained as careful follow-up is undertaken.

D. REANASTOMOSIS

Reversal of the bypass is done for a variety of reasons but is ordinarily performed because of severe complications: intractable diarrhea and weight loss, uncontrollable electrolyte imbalance, liver failure. It has been necessary to take down the bypass in 0 to 3% of reported cases, as shown in the following table:

TABLE 17
REANASTOMOSIS OF JEJUNOILEOSTOMY

SERIES	NUMBER(%)	REASON			
		MALNUTRITION	LIVER	MEGACOLON	OTHER
Scott (175)	1/ 62 (1.6%)	X			
Salmon (165)	0/120				
Buchwald (28)	1/ 94 (1%)*		X		
Fikri (52)	0/ 52+				
Weismann (217)	2/123 (1.6%)	X			X[x]
Jewell (87)	1/ 52 (2%)			X	
Payne (148)	4/140 (2.8%)				X[∓]
Benfield (20)	1/ 30 (3.3%)	X			
Starkloff (191)	4/475 (1%)		X[#]		X[‡]

* 1 other patient underwent partial refunctionalization for refractory hypocalcemia.
\+ 4/52 required partial refunctionalization to relieve intractable weight loss, diarrhea, and electrolyte imbalance.
x acute ulcerative colitis, unresponsive to therapy. Follow-up sigmoidoscopy 1 year later showed persistent ulcerative colitis.
∓ either for electrolyte imbalance or "alarming change in results of their liver function tests."
\# "secondary to psychogenic vomiting"
‡ 3 cases: patient's request; patient unable to follow post-op instructions; "glomerular nephritis."

In the present series, a similar rate of reanastomosis was seen (1%). Only one patient had her bypass taken down during what she describes as a 3-4 month hospitalization for "kidney trouble." Other indications for

reanastomosis recommended by most surgeons include the severe polyarthritis that may occur post-bypass. As was noted above, Mason and Printen propose that an atrophic small bowel mucosa be an indication for reanastomosis.[114] If patients find themselves debilitated by fatigue and lassitude despite a stable adequate weight and normal electrolytes, they may request reanastomosis.

Warren brings up a point of concern in regard to reanastomosis. He performed a feeding jejunostomy into the bypassed segment of bowel for nutrition in a woman who developed cirrhosis 2 years after jejunoileostomy. Surprisingly, he found the blind loop virtually non-functional.[175] How commonly this occurs is not known, but it does raise the question of whether the bypass procedure is in fact reversible in the long run.

E. PATIENT SATISFACTION

Solow et al investigated patient satisfaction with the bypass procedure as a whole. Of 29 patients interviewed, 23 replied that they would repeat the procedure; 4 were "tentatively satisfied"; and 2 were dissatisfied. The 2 dissatisfied patients were disappointed in the degree of weight loss achieved.[186] Benfield also found a high degree of patient satisfaction: 97-100% of his 30 patients were satisfied with the procedure. He notes, however, that only 13 of 27 were entirely asymptomatic at the time, and states that the surgeon was satisfied with the overall results in only about 50% of the cases.[20]

In this study, 23 of 29 patients voluntarily answering questionnaires replied "definitely yes" when asked if they would "do it all over again." Three said "probably yes," 3 "probably no," and 1 definitely would not repeat the procedure. There was no apparent relationship between either weight loss or the number of complications circled on the questionnaire and the patient's satisfaction with the procedure, but 3 of the 4 patients who were dissatisfied mentioned side effects as the reason.

Although patients are often ecstatic about successful weight loss, can the physician ignore the risks?[20] In subjects with serious, life-shortening complications of their obesity such as hypertension and diabetes, a strong case can be made for jejunoileostomy. Degenerative arthritis, venous stasis, job and social discrimination are also crippling, and only the patient knows just how disabling. Patient satisfaction is not physician satisfaction. As one patient stated, "If I should die ten years before my time I'd rather have had two years of being slim." It has always been the physician's responsibility to recommend the course

which is in the patient's best interest, and the case of jejunoileostomy can be no exception. As such it presents the physician with a difficult clinical judgment.

IV. SUMMARY AND CONCLUSIONS

The complications of obesity and morbid obesity have been reviewed. Of particular importance are hypertension, elevated serum cholesterol levels, diabetes mellitus, degenerative arthritis, venous stasis, and the Pickwickian syndrome. Medical management of morbid obesity does not consistently produce maintained weight loss. The most commonly performed surgical procedure for obesity is the jejunoileostomy, or intestinal bypass.

A follow-up of 93 cases of 10+8 end-to-side jejunoileostomies performed in rural Montana has been presented. Average pre-operative weight was 263 $\pm$ 6 pounds (range 162 to 466 pounds). Patients' ages varied from 16 to 61 years. There were 14 men and 79 women. Average weight loss at one year after surgery was 79 $\pm$ 4 pounds; more than two years after surgery, weight loss averaged 95 $\pm$ 6 pounds. Weight loss at one year was correlated with pre-operative weight ($r = 0.70$). A correlation was found between pre-operative systolic blood pressure and relative weight; however the correlation was much less marked when age was taken into account. Blood pressure fell significantly in both hypertensive and normotensive patients after surgery. Both systolic and diastolic pressures fell to a greater degree in patients who were hypertensive prior to surgery. A marked early decline in blood pressure in hypertensives appeared to account for the entire difference, and it is suggested that obese hypertensives may be more sensitive to changes in fluid and/or salt balance than normotensives. Although a direct relationship between weight loss and change in blood pressure could not be demonstrated, the two variables were correlated in hypertensive women on long-term follow-up. Eighteen of 28 pre-operative hypertensives (64%) became normotensive after surgery.

In terms of complications, there were 4 deaths (4.3%), all occurring within one month of surgery. One was related to a technical error and the other 3 were attributed clinically to myocardial infarction or pulmonary emboli. Morbidity in this series was comparable to that reported elsewhere, namely wound infections: 6.4%; liver disease: 2.1%; hypokalemia/hypocalcemia (requiring hospitalization): 2.1%; urinary tract stones: 3.2%. Information on complications such as liver failure, arthritis, gallstones, and anemia was not available for this report. Because of the number of patients lost to follow-up, the incidence of other complications has probably been underestimated. Four patients (4.3%) underwent revision of the bypass for inadequate weight loss. A single reanastomosis was performed because of renal impairment. There appeared to be little change in the work status of these patients, and the same number were on Welfare after surgery as before. In general patients seemed to be satisfied with the procedure: 23 of 29 who returned questionnaires stated that they would definitely "do it all over agains."

In conclusion:

(1) Morbid obesity has serious, life-shortening complications. Many of these, including hypertension, diabetes, hypercholesterolemia, and the Pickwickian syndrome, can be partially or completely reversed with weight loss.

(2) Medical management has often failed to produce permanent weight loss in the morbidly obese patient.

(3) Jejunoileostomy is a reasonable alternative to medical

management in certain cases of morbid obesity.

(4) Because of serious known complications of this procedure and a number of postulated but as yet unreported complications, strict criteria must be used in selecting patients for jejunoileostomy.

(5) These criteria include

(a) morbid obesity

(b) failure of vigorous medical management

(c) absence of correctable endocrinopathy

(d) serious complications of obesity which can be expected to improve or reverse with weight loss (including consideration of the psychosocial burden of morbid obesity).

(6) Careful follow-up after surgery is of critical importance, and patients should not be accepted for the procedure if they cannot be seen at regular intervals afterwards.

(7) Finally, it is not essential that a surgeon, internist, and psychiatrist work with each patient, nor is it necessary that the procedure be performed in a university setting. Although this may be an ideal situation, good results can be achieved in a community hospital.

APPENDIX A

QUESTIONNAIRE

GENERAL INFORMATION

Date of operation: Sex: male/female

Date of birth: Height:

Weight before operation: % over ideal weight:

Ideal weight:

Present weight:

Before surgery, when was the last time your weight was "normal"?

What is the most you have ever weighed?

What is the least you have weighed in the past ten years?

WORK HISTORY

Are you presently employed? full/part time?

Describe your job:

How long have you held this job?

Have you ever been on Welfare? When?

Please list below all the jobs you have had starting from five years before your surgery and including your present job.

Type of work	Employer	Full/part time	Salary	From mo/yr	To mo/yr

MARITAL HISTORY

Are you single/married/divorced/widowed/separated? (Circle)

How many times have you been married?
Please list years of all marriages below (example: 1953 to present).

How many children do you have?

What are their ages?

COMMUNITY ACTIVITIES

Do you belong to a church? How long have you been a member?

List any clubs or community organizations of which you are a member (Lions Club, Rotary Club, PTA, Sewing Circle, Ceramics Group, etc.). Behind each organization put the number of years you have been a member.

Have you ever been an officer or committee chairman of any church or community organization? If so, please indicate your position and the dates you held it.

HEALTH

Were any of the following a problem for you after your operation? (Underline) After each problem underlined, write how long it bothered you.

Diarrhea	Joint pains	Anemia	Weak spells
Bloating (gas)	Kidney stones	Dizziness	Vomiting
Muscle cramps	Gallstones (gallbladder disease)		Abdominal cramps

List the names of any medications you take every day:

Have you been under a doctor's care for any medical problems since your operation? If so, what?

If you had it to do all over again, would you have this operation for your weight problem? (circle one)

Definitely yes Probably yes Probably no Definitely no

COMMENTS

Thank you very much. Your cooperation is appreciated.

APPENDIX B

DETAILS OF LONGITUDINAL CHANGES IN BLOOD PRESSURE IN 21 PATIENTS

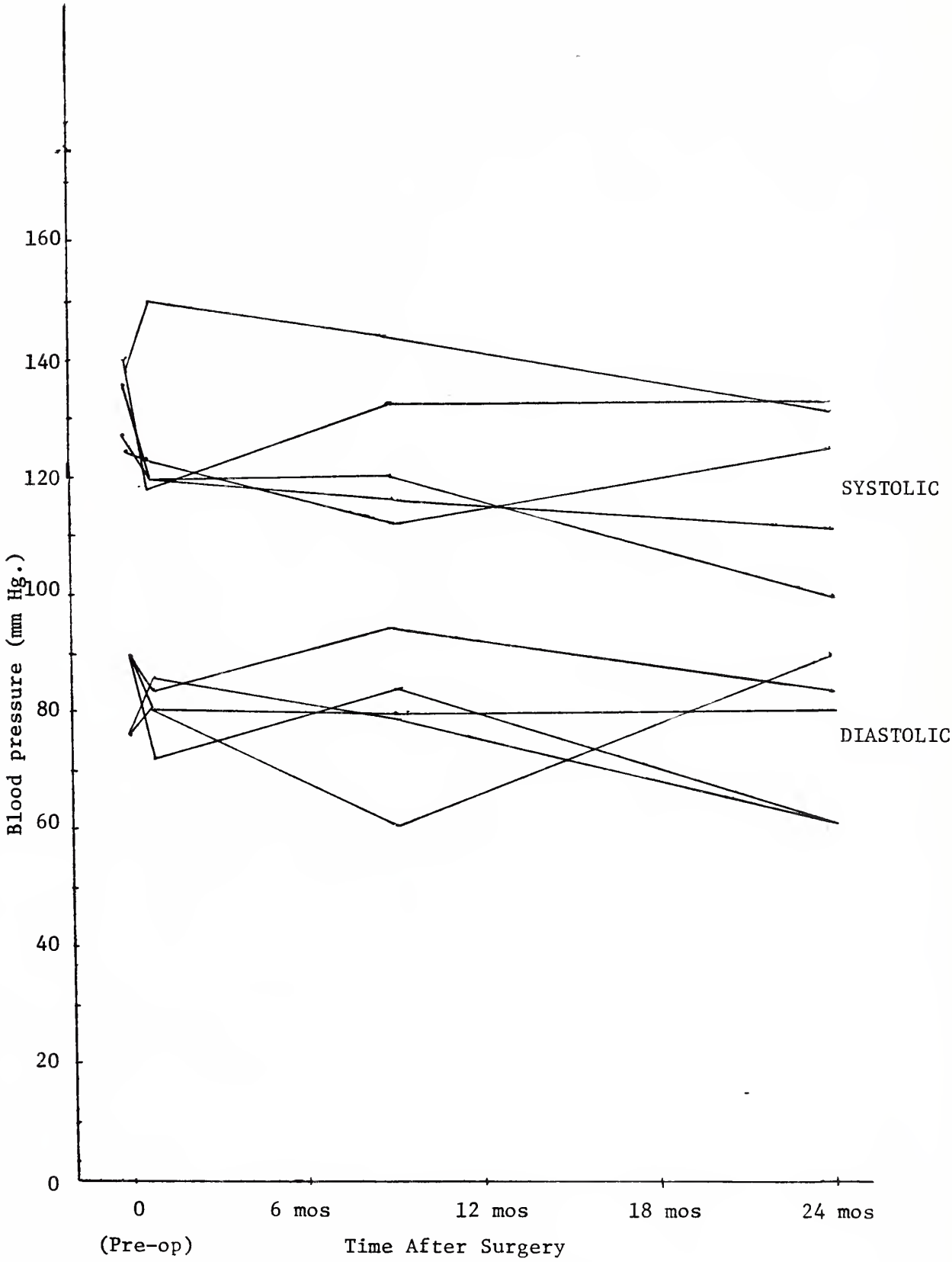

FIGURE 6A. Changes in blood pressure in 5 normotensive patients after surgery.

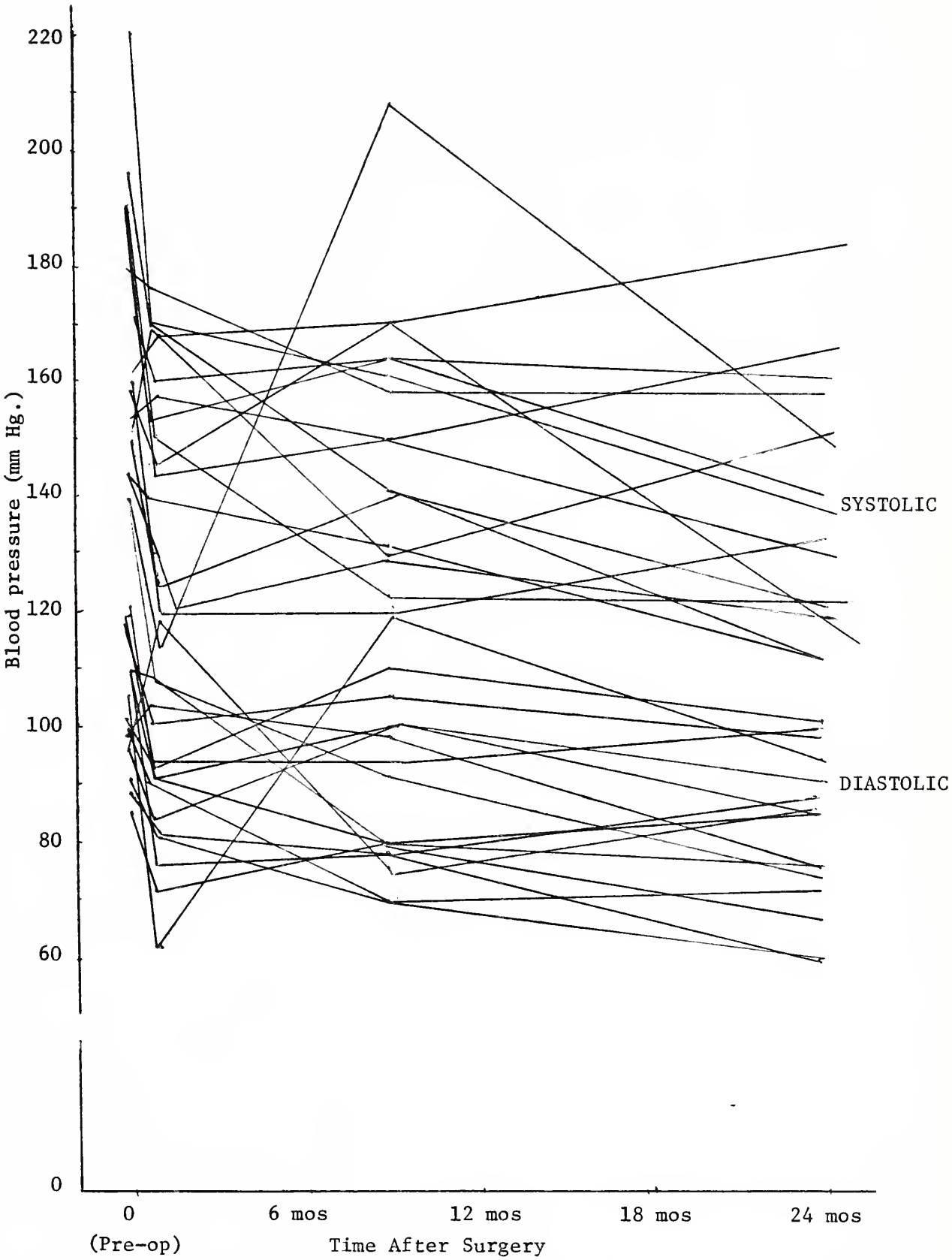

FIGURE 6B. Changes in blood pressure in 16 hypertensive patients after surgery.

APPENDIX C

PATIENT COMMENTS

"My only regret is that they didn't come out with (this) type of surgery when I was around 20 years old."

"What a wonderful feeling to walk somewhere again with my family and enjoy it!"

"I have lots of energy and feel fine mentally and physically."

"I tire very easily and wish I didn't have to work."

"I wouldn't want the weight back -- but there are also a lot of drawbacks too but I am learning to live with them."

"I am living a life that I feel would never have been my chance if not for the bypass."

"This operation has made my life."

"This operation has done a great deal for me and I certainly have not been sorry I had it done."

"Because of the surgery, my entire outlook on life and myself has changed."

"If I should die ten years before my time I'd rather have had two years of being slim."

"I am very happy with my decision..."

"I'd sure like a medication for bloating and gas."

"I now go out on dates, I can buy clothes at a regular store, people do not constantly stare and make fun of me and my size."

"Your life is changed entirely."

"Feel approximately twenty years younger."

"I feel great and had no problems."

"...to this day I have never regretted it."

"...I am now feeling better and more contented than I have for the last six years."

"My only regret is that I didn't have it sooner."

"I have been terribly sick this past year -- was hospitalized a good part of last year."

"But the effects that I have had since...are not worth it... I am not able to function properly."

"I feel 100% better."

"It has given me tomorrows that would not have been there...if there is a lessening of years ahead because of this operation at least I am grateful for the ones I've had not looking like a Sherman tank..."

BIBLIOGRAPHY

1. Alexander JK, "Chronic Heart Disease Due to Obesity," J. Chronic Dis. 18: 895-898, 1965.

2. Ashley FW, Kannel WB, "Relation of Weight Change to Changes in Atherogenic Traits: The Framingham Study," J. Chronic Dis. 27: 103-114, 1974.

3. Astwood EB, "The Heritage of Corpulence," Endocrinology 71: 337-341, 1962.

4. Bagdade JD, Bierman EL, Porte D, "The Significance of Basal Insulin Levels in the Evaluation of the Insulin Response to Glucose in Diabetic and Non-Diabetic Subjects," J.C.I. 46: 1549-1557, 1967.

5. Bar RS et al, "Fluctuations in the Affinity and Concentration of Insulin Receptors on the Circulating Monocytes of Obese Patients," J.C.I. 58: 1123-1135, 1976.

6. Barter PJ, Nestel PJ, "Precursors of Plasma Triglyceride Fatty Acids in Obesity," Metabolism 22: 779-785, 1973.

7. Battershill JH, "Tuberculosis After Intestinal Bypass Surgery for Obesity," (letter), Chest 70: 318, 1976.

8. Bennett GV, Cuatrecasas P, "Insulin Receptor of Fat Cells in Insulin-Resistant Metabolic States," Science 176: 805-806, 1972.

9. Berkowitz D, "Metabolic Changes Associated with Obesity Before and After Weight Reduction," J.A.M.A. 187: 399-403, 1964.

10. Berliner K et al, "Blood Pressure Measurements in Obese Persons," Amer. J. Card. 8: 10-17, 1961.

11. Binder HJ, "Intestinal Oxalate Absorption," Gastroenterology 66: 667 (Abstract), 1974.

12. Blackburn H, Parlin RW, "Antecedents of Disease. Insurance Mortality Experience," Ann. N.Y. Acad. Sci. 134: 965-1017, 1966.

13. Bleicher JE, Cegielski M, Saporta JA, "Intestinal Bypass Operation for Massive Obesity," Postgrad. Med. 55: 65, 1974.

14. Bortz WM, "Metabolic Consequences of Obesity," Ann. Int. Med. 71: 833-843, 1969.

15. Bortz WM, "Predictability of Weight Loss," J.A.M.A. 204: 101-105, 8 April 1968.

16. Braunstein JJ, "Management of the Obese Patient," Med. Clin. N.A. 55: 391-401, March 1971.

17. Bray GA, "Effect of Caloric Restriction on Energy Expenditure in Obese Patients," Lancet 2: 397-398, 1969.

18. Bray GA, "The Myth of Diet in the Management of Obesity," (editorial), Am. J. Clin. Nutr. 23: 1141-1148, September, 1970.

19. Bray GA, "Obesity: A Serious Symptom," Ann. Int. Med. 77: 779-795, November, 1972.

20. Bray GA et al, "Intestinal Bypass Operation as a Treatment for Obesity," Ann. Int. Med. 85: 97-109, July, 1976.

21. Brill AB et al, "Changes in Body Composition after Jejunoileal Bypass in Morbidly Obese Patients," Am. J. Surg. 123: 49-56, January, 1972.

22. Brosin HW, "The Psychology of Overeating," N.E.J.M. 248: 974-975, 4 June 1953.

23. Bruch H, "Psychiatric Aspects of Obesity," Metabolism 6: 461-465, 1957.

24. Buchanan JR, "Five Year Psychoanalytic Study of Obesity," Am. J. Psychoanal. 33: 30-38, 1973.

25. Buchwald H, "Lowering of Cholesterol Absorption and Blood Levels by Ileal Exclusion," Circ. 29: 713-720, May, 1964.

26. Buchwald H, Lober PH, Varco RL, "Liver Biopsy Findings in Seventy-Seven Consecutive Patients Undergoing Jejunoileal Bypass for Morbid Obesity," Am. J. Surg. 127: 48, January, 1974.

27. Buchwald H, Moore RB, Varco RL, "Surgical Treatment of Hyperlipidemia. III. Clinical Status of the Partial Ileal Bypass Operation," Circ. 49 (Suppl. I): I23-I37, 1974.

28. Buchwald H, Schwartz MZ, Varco RL, "Surgical Treatment of Obesity," Adv. Surg. 7: 235-255, 1973.

29. Burcher SK, Sorrell VF, "Intestinal Bypass for Obesity," New Zealand Medical Journal 73: 129, 1971.

30. Burwell CS et al, "Extreme Obesity Associated with Alveolar Hypoventilation -- A Pickwickian Syndrome," Am. J. Med. 21: 811-818, November, 1956.

31. Carey JB et al, "The Metabolism of Bile Acids with Special Reference to Liver Injury," Medicine 45: 461-470, 1966.

32. Castelnuovo-Tedesco P, Schiebel D, "Studies of Superobesity: II. Psychiatric Appraisal of Jejuno-Ileal Bypass Surgery," Am. J. Psych. 133: 26-31, January 1976.

33. Chapman JM et al, "The Differential Effect of Serum Cholesterol, Blood Pressure, and Weight on the Incidence of Myocardial Infarction and Angina Pectoris," J. Chron. Dis. 23: 631-645, 1971.

34. Charney E et al, "Childhood Antecedents of Adult Obesity," N.E.J.M. 295: 6, 1 July 1976.

35. Chiang BN, Perlman LV, Epstein FH, "Obesity and Hypertension," Circ. 49: 403-421, 1969.

36. Chirico AM, Stunkard AJ, "Physical Activity and Human Obesity," N.E.J.M. 263: 935-940, 10 November 1960.

37. Clark PJ, "The Heritability of Certain Anthropometric Characters as Ascertained from Measurements of Twins," Am. J. Hum. Gen. 8: 49-54, 1956.

38. Coyle JJ, Varco RL, Buchwald H, "Gastric Secretion and Serum Gastrin in Human Small Bowel Bypass," Arch. Surg. 110:1036-1038, 1975.

39. Crisp, AH et al, "Sleep Patterns in Obese Patients during Weight Reduction," Psychother. and Psychosom. 22: 159-165, 1973.

40. Cryer PE et al, "Renal Failure After Small Intestinal Bypass for Obesity," Arch. Int. Med. 135: 1610-1612, 1975.

41. Dahl, LK, Silver L, Christie RW, "The Role of Salt in the Fall of Blood Pressure Accompanying Reduction in Obesity," N.E.J.M. 258: 1186-1192, 1958.

42. DeFronzo RA et al, "The Effect of Insulin on Renal Handling of Sodium, Potassium, Calcium, and Phosphate in Man," J.C.I. 55: 845-855, 1975.

43. DeMeyts P, Roth J et al, "Insulin Interactions with Its Receptors: Experimental Evidence for Negative Cooperativity," Biochem. Biophys. Res. Comm. 55: 154-161, 1973.

44. DeMuth WE, Rottenstein HS, "Death Associated with Hypocalcemia After Small-Bowel Short Circuiting," N.E.J.M. 270: 1239-1240, 1964.

45. DeWind LT, Payne JH, "Intestinal Bypass Surgery for Morbid Obesity: Long-term Results," J.A.M.A. 236: 2298-2301, 1976.

46. "Drastic Cures for Obesity," (editorial), Lancet 1: 1094, 23 May 1970.

47. Drenick EJ, Simmons F, Murphy JF, "Effect on Hepatic Morphology of Treatment of Obesity by Fasting, Reducing Diets and Small-Bowel Bypass," N.E.J.M. 282: 829-834, 9 April 1970.

48. Farquhar JW et al, "Obesity, Insulin, and Triglycerides," in Obesity in Perspective, GA Bray, ed., NIH, Bethesda, Maryland, Chapter 40, pp. 313-319, 1975. DHEW Publication No. (NIH) 75-708.

49. Feinstein AR, "The Measurement of Success in Weight Reduction," J. Chron. Dis. 10: 439-456, November 1959.

50 Feinstein AR, "The Treatment of Obesity: An Analysis of Methods, Results, and Factors Which Influence Success," J. Chron. Dis. 11: 349-393, April, 1960.

51. Feinstein AR, Dole VP, Schwartz, L, "The Use of a Formula Diet for Weight Reduction of Obese Out-Patients," Ann. Int. Med. 48: 330-343, February 1958.

52. Fikri, E, Cassella R, "Jejunoileal Bypass for Massive Obesity: Results and Complications in Fifty-two Patients," Ann. Surg. 179:460-464, 1974.

53. Fletcher AP, "The Effect of Weight Reduction Upon the Blood Pressure of Obese Hypertensive Women," Quart. J. Med. 23: 331-345, 1959.

54. Fletcher RF et al, "Magnesium Deficiency Following Massive Intestinal Resection," Lancet 1: 522-525, 5 March 1960.

55. Forbes GB, Reina JC, "Adult Lean Body Mass Declines with Age: Some Longitudinal Observations," Metabolism 19: 653-663, 1970.

56. Ford S, Bozian RC, Knowles HC, "Interactions of Obesity, and Glucose and Insulin Levels in Hypertriglyceridemia," Am. J. Clin. Nutr. 21: 904-910, September 1968.

57. Freter R, Gangarosa EJ, "Oral Immunization and Production of Coproantibody in Human Volunteers," J. Immun. 91: 724-729, 1963.

58. Fried PI et al, "Effect of Ketosis on Respiratory Sensitivity to Carbon Dioxide in Obesity," N.E.J.M. 294: 1081-1086, 13 May 1976.

59. Galton DJ, Bray GA, "Metabolism of α-Glycerol Phosphate in Human Adipose Tissue in Obesity," J. Clin. Endo. Metab. 27: 1573-1580, 1967.

60. Garn SM, Haskell JA, "Fat Thickness and Developmental Status in Childhood and Adolescence," Am. J. Dis. Child. 99: 746-751, 1960.

61. Genuth SM, "Plasma Insulin and Glucose Profiles in Normal, Obese and Diabetic Persons," Ann. Int. Med. 79: 812-822, 1973.

62. Genuth SM, Castro JH, Vertes V, "Weight Reduction in Obesity by Outpatient Semi-Starvation," J.A.M.A. 230: 987-991, 1974.

63. Glennon JA, "Weight Reduction -- An Enigma," Arch. Int. Med. 118: 1-2, 1966.

64. Glucksman ML, Hirsch J, "The Response of Obese Patients to Weight Reduction: I.A Clinical Evaluation of Behavior," Psychosom. Med. 30: 1-11, 1968.

65. Glucksman ML et al,"The Response of Obese Patients to Weight Reduction: II. A Quantitative Evaluation of Behavior," Psychosom. Med. 30: 359-373, 1968.

66. Goldblatt PB, Moore ME, Stunkard AJ, "Social Factors in Obesity," J.A.M.A. 192: 1039-1044, 1965.

67. Goldman AG, Varady PD, Franklin SS, "Body Habitus and Serum Cholesterol in Essential Hypertension and Renovascular Hypertension," J.A.M.A. 221: 378-383, 24 July 1972.

68. Gurney R, "The Hereditary Factor in Obesity," Arch. Int. Med. 57: 557-561, 1936.

69. Guzman IJ, Varco RL, Buchwald H, "Factors Determining Weight Loss After Jejunoileal Bypass for Obesity," J. Surg. Res. 18: 399-403, 1975.

70. Hackney JD et al, "Syndrome of Extreme Obesity and Hypoventilation: Studies of Etiology," Ann. Int. Med. 51: 541-552, 1959.

71. Hall SM, "Behavioral Treatment of Obesity: A Two-year Follow-up," Behav. Res. Ther. 11: 647-648, 1973.

72. Hallberg D, Backman L, "Kinetics of Body Weight After Intestinal Bypass Operations in Obesity," Acta Chir. Scand. 139: 557-562, 1973.

73. Hamburger WW, "Emotional Aspects of Obesity," Med. Clin. N.A. 35: 483-499, 1951.

74. Harmon JW, Aliapoulos M, Braasch JW, "The Excluded Small-Bowel Segment," Arch. Surg. 111: 953-954, 1976.

75. Hawkins WW, "Some Medical and Biological Aspects of Obesity," Canad. J. Public Health 54: 477-481, 1963.

76. Heyden S et al, "Decrease of Serum Cholesterol Level and Blood Pressure in the Community," Arch. Int. Med. 128: 982-986, 1971.

77. Heyden S et al, "Weight and Weight History in Relation to Cerebrovascular and Ischemic Heart Disease," Arch. Int. Med. 128: 956-964, 1971.

78. Hirsch J, Van Itallie TB, "The Treatment of Obesity," (letter), Am. J. Clin. Nutr. 26: 1039-1041, 1973.

79. Hofmann AF, Poley JR, "Cholestyramine Treatment of Diarrhea Associated with Ileal Resection," N.E.J.M. 281: 397-402, 1969.

80. Holland WW, Humerfelt S, "Measurement of Blood Pressure: Comparison of Intra-arterial and Cuff Values," B.M.J. 2: 1241-1243, 14 November 1964.

81. Hollenbeck JI et al, "Liver Scan as a Measure of Liver Function Following Jejunoileal Bypass for Morbid Obesity," Surg. Forum 24: 402-404, 1973.

82. Hollister LE, Overall JE, Snow HL, "Relationship of Obesity to Serum Triglyceride, Cholesterol, and Uric Acid, and to Plasma-Glucose Levels," Am. J. Clin. Nutr. 20: 777-782, 1967.

83. Holzbach RT et al, "Hepatic Lipid in Morbid Obesity," N.E.J.M. 290: 296-299, 7 February 1974.

84. Hunscher MA, "A Posthospitalization Study of Patients Treated for Obesity by a Total Fast Regimen," Metab. 15: 383-393, 1966.

85. "Hypotensive Effect of Fenfluramine in the Treatment of Obesity," Practitioner 207: 101-105, 1971.

86. Jelliffe RW et al, "Death from Weight-Control Pills," J.A.M.A. 208: 1843-1847, 9 June 1969.

87. Jewell WR, "Complications of Jejunoileal Bypass for Morbid Obesity," Arch. Surg. 110: 1039-1042, August 1975.

88. Johnson CD, Bynum TE, "Hypocalcemia as a Complication of Jejunoileal Bypass for Morbid Obesity," South. Med. J. 69: 616-618, 1976.

89. Johnson ML, Burke, BS, Mayer, J, "Relative Importance of Inactivity and Overeating in the Energy Balance of Obese High School Girls," Am. J. Clin. Nutr. 4: 37-44, 1956.

90. Kalisch B, "The Stigma of Obesity," Am. J. Nursing 72: 1124-1127, 1972.

91. Kannel WB et al, "The Framingham Study. The Relation of Adiposity to Blood Pressure and Development of Hypertension," Ann. Int. Med. 67: 48-59, 1967.

92. Kannel WB et al, "The Framingham Study. Relation of Body Weight to Development of Coronary Heart Disease," Circ. 35: 734, 1967.

93. Karam JH, Grodsky GM, Forsham PH, "Excessive Insulin Response to Glucose in Obese Subjects as Measured by Immunochemical Assay," Diabetes 12: 197-204, 1963.

94. Kaufmann HJ, Weldon HW, "Intussusception: A Late Complication of Small-Bowel Bypass for Obesity," J.A.M.A. 202: 87-88, 1967.

95. Keck, C, "Obesity and Orthopedics," J. Amer. Med. Women's Assoc. 19: 759-760, 1964.

96. Kern WH et al, "Fatty Metamorphosis of the Liver in Morbid Obesity," Arch. Path. 96: 342-346, 1973.

97. Keys A, Brozek J, "Overweight versus Obesity and the Evaluation of Calorie Needs," Metab. 6: 425-434, 1957.

98. Keys A et al, "Coronary Heart Disease: Overweight and Obesity as Risk Factors," Ann. Int. Med. 77: 15-27, 1972.

99. Keys A, Henschel A, Taylor HL, "The Size and Function of the Human Heart at Rest in Semi-Starvation and in Subsequent Rehabilitation," Am. J. Phys. 150: 153-169, 1947.

100. Kremen AJ, Linner JH, Nelson CH, "An Experimental Evaluation of the Nutritional Importance of Proximal and Distal Small Intestine," Ann. Surg. 140: 439-448, 1954.

101. Lawlor T, Wells DG, "Metabolic Hazards of Fasting," Am. J. Clin. Nutr. 22: 1142-1149, 1969.

102. Leevy CM, "Fatty Liver: A Study of 270 Patients with Biopsy Proven Fatty Liver and a Review of the Literature," Medicine 41: 249-278, 1962.

103. LeVeen HH et al, "Cause and Treatment of Diarrhea Following Resection of the Small Intestine," Surg. Gyn. Ob. 124: 766-770, 1967.

104. Lewis LA, Turnball RB, Page IH, "Effects of Jejunocolic Shunt on Obesity, Serum Lipoproteins, Lipids, and Electrolytes," Arch. Int. Med. 117: 4-16, 1966.

105. Lewis LA, Turnball RB, Page IH, " 'Short-Circuiting' of the Small Intestine," J.A.M.A. 182: 77-79, 6 October 1962.

106. MacCuish AC, Munro JF, Duncan LJP, "Follow-up Study of Refractory Obesity Treated by Fasting," B.M.J. 1: 91-92, 13 January 1968.

107. Maeder EC et al, "Obesity: A Maternal High-Risk Factor," Obstetrics and Gynecology 45: 669-671, 1975.

108. Malt RA, Guggenheim FG, "Surgery for Obesity," (editorial), N.E.J.M. 295: 43, 1976.

109. Mann GV, "The Influence of Obesity in Health," N.E.J.M. 291: 178-185,226-232, 1974.

110. Mann GV, "Obesity, the Nutritional Spook," Am. J. Public Health 61: 1491-1498, 1971.

111. Marks HH, "Influence of Obesity on Morbidity and Mortality," Bull. N. Y. Acad. Med. 36: 296-312, 1960.

112. Martin L, "The Effect of Weight Reduction on Normal and Raised Blood Pressures in Obesity," Lancet 2: 1051-1053, 1952.

113. Mason EE,"Obesity is a Surgical Dilemma," Surg. Gun. Ob. 138: 425-426, 1974.

114. Mason EE, Printen KJ, "Metabolic Considerations in Reconstitution of the Small Intestine After Jejunoileal Bypass," Surg. Gyn. Ob. 142: 177-183, 1976.

115. Mason EE et al, "Fatty Acid Toxicity," Surg. Gyn. Ob. 133: 992-998, 1971.

116. Master AM, Jaffe HL, Chesky K, "Relationship of Obesity to Coronary Disease and Hypertension," J.A.M.A. 153: 1499-1501, 1953.

117. Master AM, Oppenheimer ET, "A Study of Obesity: Circulatory, Roentgen-Ray, and Electrocardiographic Investigations," J.A.M.A. 92: 1652-1656, 1929.

118. Mayer J, " Genetic, Traumatic and Environmental Factors in the Etiology of Obesity," Physiol. Rev. 33: 472-508, 1953.

119. Mayer J, "Some Advances in the Study of the Physiologic Basis of Obesity," Metab. 6: 435-446, 1957.

120. Mayer J, Roy P, Mitra KP, "Relation Between Caloric Intake, Body Weight, and Physical Work: Studies in an Industrial Male Population in West Bengal," Am J. Clin. Nutr. 4: 169-175, 1956.

121. McGee V, Principles of Statistics: Traditional and Bayesian, Meredith Corporation, New York, 1971.

122. Mezey E et al, "Endogenous Ethanol Production and Hepatic Disease Following Jejunoileal Bypass for Morbid Obesity," Am. J. Clin. Nutr. 28: 1277-1283, 1975.

123. Miller DS, Mumford P, "Gluttony I. An Experimental Study of Overeating Low- or High-Protein Diets," Am. J. Clin. Nutr. 20: 1212-1222, 1967.

124. Miller DS, Mumford P, Stock MJ, "Gluttony 2. Thermogenesis in Overeating Man," Am. J. Clin. Nutr. 20: 1223-1229, 1967.

125. Montoye HJ, Epstein FH, Kjelsberg MO, "Relationship Between Serum Cholesterol and Body Fatness," Am. J. Clin. Nutr. 18: 397-406, 1966.

126. Moxley RT, Pozefsky T, Lockwood DH, "Protein Nutrition and Liver Disease After Jejunoileal Bypass for Morbid Obesity," N.E.J.M. 290: 921-926, 1974.

127. Mulcare DB, Dennin HF, Drenick EJ, "Effect of Diet on Malabsorption After Small-Bowel Bypass," J. Am. Diet. Assoc. 57: 331-334, 1970.

128. Munro JF, MacCuish AC et al, "Further Experience with Prolonged Therapeutic Starvation in Gross Refractory Obesity," B.M.J. 4: 712-714, 19 December 1970.

129. Neshat AA, Flye MW, "Early Formation of Gallstones Following Jejunoileal Bypass for Treatment of Morbid Obesity," Am. Surg. 41: 486-491, 1975.

130. Nestel PJ, Carroll KF, Havenstein N, "Plasma Triglyceride Response to Carbohydrates, Fats, and Caloric Intake," Metab. 19: 1-18, 1970.

131. Nestel PJ, Whyte HM, "Plasma Free Fatty Acid and Triglyceride Turnover in Obesity," Metab. 17: 1122-1128, 1968.

132. "Obesity, Jejunoileal Bypass and Death," Nutr. Rev. 9: 38-40, 1975.

133. O'Leary JP, Thomas WC, Woodward ER, "Urinary Tract Stone After Small Bowel Bypass for Morbid Obesity," Am. J. Surg. 127: 142-147, 1974.

134. O'Leary JP et al, "Pathogenesis of Hepatic Failure Following Jejunoileal Bypass," (Abstract), Gastroenterology 66: 859, April 1974.

135. Olefsky JM, "Decreased Insulin Binding to Adipocytes and Circulating Monocytes from Obese Subjects," J.C.I. 57: 1165-1172, 1976.

136. Olefsky JM, "Effects of Fasting on Insulin Binding, Glucose Transport, and Glucose Oxidation in Isolated Rat Adipocytes," J.C.I. 58: 1450-1460, 1976.

137. Olefsky JM, "The Effects of Spontaneous Obesity on Insulin Binding, Glucose Transport, and Glucose Oxidation of Isolated Rat Adipocytes," J.C.I. 57: 842-851, 1976.

138. Olefsky JM, "The Insulin Receptor: Its Role in Insulin Resistance of Obesity and Diabetes," Diabetes 25: 1154-1162, December 1976.

139. Olefsky JM, Reaven GM, Farquhar JW, "Effects of Weight Reduction on Obesity: Studies of Lipid and Carbohydrate Metabolism in Normal and Hyperlipoproteinemic Subjects," J.C.I. 53: 64-76, 1974.

140. Olson RE, "Obesity as a Nutritional Disorder," Fed. Proc. 18: (Part I) 58-67, 1959.

141. "Operations for Obesity," (editorial), B.M.J. 4: 247, 30 October 1971.

142. Orma E, Karvonen MJ, Keys A, " 'Cuff' Hypertension," (letter), Lancet 2: 51, 2 July 1960.

143."Overweight: Its Prevention and Significance," Statistical Bulletin, Metropolitan Life Insurance Company, 1960.

144. Owens RL, Jones AL, "Epithelial Cell Specialization Within Human Peyer's Patches: An Ultrastructural Study of Intestinal Lymphoid Follicles," Gastro. 66: 189-203, 1974.

145. Passaro E, Drenick E, Wilson SE, "Bypass Enteritis," Am. J. Surg. 131: 169-174, 1976.

146. Payne JH, DeWind LT,"Surgical Treatment of Obesity," Am. J. Surg. 118: 141-147, 1969.

147. Payne JH, DeWind LT, Commons RR, "Metabolic Pbservations in Patients with Jejunocolic Shunts," Am. J. Surg. 106: 273-289, 1963.

148. Payne JH et al,"Surgical Treatment of Morbid Obesity: Sixteen Years of Experience," Arch. Surg. 106: 432-437, 1973.

149. Penick SB et al, "Behavior Modification in the Treatment of Obesity," Psychosom. Med. 33: 49-55, 1971.

150. Perley M, Kipnis DM, "Plasma Insulin Repsonses to Glucose and Tolbutamide of Normal Weight and Obese Diabetic and Nondiabetic Subjects," Diabetes 15: 867-874, 1966.

151. Peters RL, Gay T, Reynolds TB, "Post-jejunoileal-bypass Hepatic Disease," Am. J. Clin. Path. 63: 318, 1975.

152. Pickleman JR et al, "Tuberculosis After Jejunoileal Bypass for Obesity," J.A.M.A. 234: 744, 1975.

153. Powdermaker H, "An Anthropological Approach to the Problem of Obesity," Bull. N.Y. Acad. Med. 36: 286-295, 1960.

154. Preble WE, "Obesity: Observations on One Thousand Cases," Bost. Med. Surg. J. 188: 617-621, 1923.

155. Printen KJ, Mason EE, "Fastric Surgery for Relief of Morbid Obesity," Arch. Surg. 106: 428-431, 1973.

156. Quaade F et al, "Blind Loop Reflux in Relation to Weight Loss in Obese Patients Treated with Jejunoileal Anastomosis," Scand. J. Gastro. 6: 537-541, 1971.

157. Quereshi MY, "Some Behavioral and Biosocial Correlates of Remediability Among the Chronically Obese," J. Clin. Psych. 31: 103-107, 1975.

158. Ravelli GP et al, "Obesity in Young Men After Famine Exposure in Utero and Early Infancy," N.E.J.M. 295: 349-353, 1976.

159. Resnick M, Joubert L, "A Double-Blind Evaluation of an Anorexiant, a Placebo, and Diet Alone in Obese Subjects," Canad. Med. Assoc. J. 97: 1011-1015, 1967.

160. Rivlin RS, "Therapy of Obesity with Hormones," N.E.J.M. 292: 26-29, 1975.

161. Rochester DF, Enson Y, "Current Concepts in the Pathogenesis of the Obesity-Hypoventilation Syndrome," A.J. Med. 57: 402-420, 1974.

162. Rodin J,"The Responsiveness of the Obese to External Stimuli," in Obesity in Perspective, GA Bray, ed., NIH, Bethesda, Maryland, Volume 2, Part 2, pp. 61-71, 1975. DWEH Publication Number (NIH) 75-708.

163. Rozental P et al, "Liver Morphology and Function Tests in Obesity and During Total Starvation," Am. J. Dig. Dis. 12: 198-208, 1967.

164. Salans LB, Knittle JL, Hirsch J, "The Role of Adipose Cell Size and Adipose Tissue Insulin Sensitivity in the Carbohydrate Intolerance of Human Obesity," J.C.I. 47: 153-165, 1968.

165. Salmon PA, "The Results of Small Intestine Bypass Operations for the Treatment of Obesity," Surg. Gyn. Ob. 132: 965-979, 1971.

166. Salzano JV et al, "Effect of Weight Loss on Blood Pressure," J. Am. Diet. Assoc. 34: 1309-1312, 1958.

167. Saudek CD, Boulter PR, Arky RA, "The Natriuretic Effect of Glucagon and its Role in Starvation," J.C.E.M. 36: 761-765, 1973.

168. Schachter S, "Some Extraordinary Facts About Obese Humans and Rats," Amer. Psych. 26: 129-144, 1971.

169. Scheck J et al, "Mineral and Protein Losses During Starvation," J. Am. Diet. Assoc. 49: 211-214, 1966.

170. Schick A, "Psychosomatic Aspects of Obesity," Psychoanalytic Review 34: 173-183, 1947.

171. Schwartz H, Jensen H, "Jejunoileostomy in the Treatment of Obesity," Acta Chir, Scand. 139: 551-556, 1973.

172. Scott HW, Law DH, "Clinical Appraisal of Jejunoileal Shunts in Patients with Morbid Obesity," Am. J. Surg. 117: 247-253, 1969.

173. Scott HW et al, "Experience with a New Technique of Intestinal Bypass in the Treatment of Morbid Obesity," Ann. Surg. 174: 560-572, 1971.

174. Scott HW et al, "Jejunoileal Shunt in Surgical Treatment of Morbid Obesity," Ann. Surg. 171: 770-782, 1970.

175. Scott HW et al, "New Considerations in Use of Jejunoileal Bypass in Patients with Morbid Obesity," Ann. Surg. 177: 723-735, 1973.

176. Sebrell WH Jr, "Metabolic Aspects of Obesity: Facts, Fallacies, and Fables," Metab. 6: 411-416, 1957.

177. Sedgwick CE, Goodman AA, "Short Bowel Syndrome," Surg. Clin. N. A. 51: 675-680, 1971.

178. Seltzer CC, Mayer J, "Body Build and Obesity -- Who Are the Obese?" J.A.M.A. 189: 677-684, 1964.

179. Shagrin JW, Frame B, Duncan H, "Polyarthritis in Obese Patients with Intestinal Bypass," Ann. Int. Med. 75: 377, 1971,.

180. Sherman CD et al, "Clinical and Metabolic Studies Following Bowel Bypassing for Obesity," Ann. N.Y. Acad. Sci. 131: 614-622, 1965.

181. Sigler MH, "The Mechanism of the Natriuresis of Fasting," J.C.I. 55: 377-387, 1975.

182. Silverstone JT, Solomon T, "The Long-term Management of Obesity in General Practice," Brit. J. Clin. Pract. 19: 395-398, 1965.

183. Sims EAH, Horton ES, Salans LB, "Inducible Metabolic Abnormalities During the Development of Obesity," Annual Review of Medicine 22: 235-250, 1971.

184. Siperstein MD, "The Glucose Tolerance Test: A Pitfall in the Diagnosis of Diabetes Mellitus," Adv. Int. Med. 20: 297-323, 1975.

185. Sohar E, Sneh E, "Follow-up of Obese Patients: 14 Years After A Successful Reducing Diet," Am. J. Clin. Nutr. 26: 845-848, 1973.

186. Solow C, Silberfarb PM, Swift K, "Psychosocial Effects of Intestinal Bypass Surgery for Severe Obesity," N.E.J.M. 290: 300-303, 1974.

187. Sorrell VF, Knight DH, Burcher SK, "Pancreatitis Following Intestinal Bypass for Obesity," The Austr. New Zeal. J. Surg. 45: 163-167, 1975.

188. Soyer MT, Ceballos R, Aldrete JS, "Reversibility of Severe Hepatic Damage Caused by Jejunoileal Bypass After Re-establishment of Normal Intestinal Continuity," Surg. 79: 601-604, 1976.

189. Spark RF et al, "Renin, Aldosterone, and Glucagon in the Natriuresis of Fasting," N.E.J.M. 292: 1335-1340, 1975.

190. Spencer IOB, Durh MB, "Death During Therapeutic Starvation for Obesity," Lancet 1: 1288-1290, 15 June 1968.

191. Starkloff GB et al, "Metabolic Intestinal Surgery: Its Complications and Management," Arch. Surg. 110: 652-657, 1975.

192. Stewart IM, "Long-term Observations on High Blood Pressure Presenting in Fit Young Men," Lancet 1: 355-358, 1971.

193. Stonehill E, Crisp AH, "Aspects of the Relationship between Sleep, Weight, and Mood," Psychother. and Psychosom. 22: 148-158, 1973.

194. Stuart RB, "Behavioral Control of Overeating," Behav. Res. Ther. 5: 357-365, 1967.

195. Stuart RB, "A Three-Dimensional Program for the Treatment of Obesity," Behav. Res. Ther. 9: 177-186, 1971.

196. Stunkard AJ, "The 'Dieting Depression' ", Am. J. Med. 23: 77-86,1957.

197. Stunkard AJ, "New Therapies for the Eating Disorders," Arch. Gen. Psych. 26: 391-398, 1972.

198. Stunkard AJ, "Obesity and the Denial of Hunger," Psychosom. Med. 21: 281-289, 1959.

199. Stunkard AJ, Burt V, "Obesity and the Body Image: II. Age at Onset of Disturbances in the Body Image," Am. J. Psych. 123: 1443-1447, 1967.

200. Stunkard AJ, McLaren-Hume M, "The Results of Treatment for Obesity," Arch. Int. Med. 103: 79-85, 1959.

201. Stunkard AJ, Mendelson M, "Obesity and the Body Image: I. The Characteristics of the Body Image of Some Obese Persons," Am. J. Psych. 123: 1296-1300, 1967.

202. "Surgery for Severe Obesity," (editorial), B.M.J. 2: 575, 15 June 1974.

203. Swanson DW, Dinello FA, "Follow-up of Patients Starved for Obesity," Psychosom. Med. 32: 209-214, 1970.

204. Swanson DW, Dinello FA, "Severe Obesity as a Habituation Syndrome," Arch. Gen. Psych. 22: 120-127, 1970.

205. Ten State Nutrition Survey, 1968-1970, Volume III, U.S. Dept. HEW, 1972. DHEW Publication Number (HSM) 72-8131.

206. Terry AH, "Obesity and Hypertension," J.A.M.A. 81: 1283-1284, 1923.

207. Thorn GW, Cahill GF, "Gain in Weight. Obesity." in Harrison's Principles of Internal Medicine, Wintrobe, ed., MacGraw-Hill, New York, Chapter 45, pp. 232-236, 1974.

208. U.S. Public Health Service, Division of Chronic Diseases: Obesity and Health. PHS Publication No. 1485, Washington, D.C., U.S. Govt. Printing Office, 1966.

209. Vainder M, Kelly J, "Renal Tubular Dysfunction Secondary to Jejunoileal Bypass," J.A.M.A. 235: 1257-1258, 1976.

210. Waal-Manning HJ, Simpson FO, "Fenfluramine in Obese Patients on Various Antihypertensive Drugs," Lancet 2: 1392-1395, 1969.

211. Wagonfield S, Wolowitz HM, "Obesity and the Self-Help Group: A Look at TOPS," Am. J. Psych. 125: 249-252, 1968.

212. Wands JR et al, "Arthritis Associated With Intestinal Bypass Procedure for Morbid Obesity," N.E.J.M. 294: 121-124, 1976.

213. Warlow CP, "Platelet Adhesiveness, Coagulation, and Fibrinolytic Activity in Obesity," J. Clin. Path. 25 : 484-486, 1972.

214. Weinsier RL, "Fasting -- A Review With Emphasis on the Electrolytes," Am. J. Med. 50: 233-240, 1971.

215. Weinsier RL et al, "Body Fat: Its Relationship to Coronary Heart Disease, Blood Pressure, Lipids, and Other Risk Factors Measured in a Large Male Population," Am. J. Med. 61: 815-824, 1976.

216. Weisinger JR et al, "The Nephrotic Syndrome: A Complication of Massive Obesity," Ann. Int. Med. 81: 440-447, 1974.

217. Weismann R, "Surgical Palliation of Massive and Severe Obesity," Am. J. Surg. 125: 437-446, 1973.

218. Westwater JO, Fainer D, "Liver Impairment in the Obese," Gastro. 34: 686-693, 1958.

219. Whyte HM, "Blood Pressure and Obesity," Circ. 19: 511-516, 1959.

220. Wilmore DW, Pruitt BA, "Fat Boys Get Burned," Lancet 2: 631-632,1972.

221. Wilmore DW et al, "The Role of Nutrition in the Adaptation of the Small Intestine After Massive Resection," Surg. Gyn. Ob. 132: 673-680, 1971.

222. Wise L, Margraf H, Stein T, "Studies on Bile Salt Deconjugation Following Small Bowel Bypass Procedures," Ann. Surg. 181: 397-401, 1975.

223. Wise L, Stein T, "Biliary and Urinary Calculi," Arch. Surg. 110: 1043-1047, 1975.

224. Wollersheim JP, "Effectiveness of Group Therapy Based Upon Learning Principles in the Treatment of Overweight Women," J. Abnormal Psych. 76: 462-474, 1970.

225. Yang M, Van Itallie TB, "Composition of Weight Loss During Short-Term Weight Reduction," J.C.I. 58: 722-730, 1976.

226. Young CM et al, "The Problem of the Obese Patient," J. Am. Diet. Assoc. 31: 1111-1115, 1955.

227. Yudkin J, "The Causes and Cure of Obesity," Lancet 2: 1135-1138, 1959.

228. Zelman S, "The Liver in Obesity," Arch. Int. Med. 90: 141-156, 1952.

229. Zwillich CW et al, "Decreased Hypoxic Ventilatory Drive in the Obesity-Hypoventilation Syndrome," Am. J. Med. 59: 343-348, 1975.

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